CATALYTIC OXIDATION OF ALKANES AND ALKENES BY
AN AMIDE PEROXIDE SYNTHESIZED BY
THE AIR OXIDATION OF
1-METHYL-2-PYRROLIDINONE

BY

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A DISSERTATION PRESENTED TO THE GRADUATE SCHOOL
OF THE UNIVERSITY OF FLORIDA IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA

1989

ACKNOWLEDGEMENTS

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August, 1989

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The formation of two products during the oxidation of 1-methyl
2-pyrrolidinone by molecular oxygen is investigated. The two products are
determined to be the 1-methyl-5-peroxy-2 pyrrolidinone and
N-methylsuccinimide by NMR, GC-MS and infrared spectroscopy. The
oxidation reaction favors the peroxide at low temperatures (<80°C) and the
succinimide at higher temperatures.

The peroxide yield is measured at 75°C and found to be 67% in moles
peroxide per mole of molecular oxygen consumed. When this same solution is
deaerated with argon and placed in an oil bath at 75°C with
triphenylphosphine, the triphenylphosphine is oxidized totriphenylphosphine
oxide with a 40% efficiency relative to the peroxide (moles triphenylphosphine
oxide/mole peroxide).

The ability of the peroxide to epoxidize alkenes and to oxidize alkanes and alkyl sulfides is described. The 1-methyl-5-peroxy-2 pyrrolidinone was investigated in order to find its usefulness in the oxidation of organic substrates such as alkenes and sulfides. The oxidation of alkenes, alkanes and alkyl sulfides was performed in the presence of a variety of catalyst and 1-methyl-5-peroxy-2 pyrrolidinone was discovered to be a good source of peroxides for low-temperature oxidations. The system can also be used to help understand the cytochrome P-450 oxidation shunt in nature. A model system which replicates the coordinated amino-acid proline, in the structure of cytochrome P-450, is described and is demonstrated to form a peroxide at low temperatures. Acylated L-prolinamide reacted at 50°C with molecular oxygen is used to model the reactivity of the amino acid, L-proline, when it is incorporated into cytochrome P-450. The formation of a peroxide from the acylated L-prolinamide provides an alternate mechanism for the oxidation of organic substrates by natural oxidases in biological systems.

CHAPTER 1
INTRODUCTION

The oxidation of 1-methyl-2-pyrrolidinone at low temperatures to form an oxidizer was explored to identify the oxidizing species and to determine whether or not it could be used in the oxidation of alkenes and alkyl sulfides. The formation of an amide peroxide from the 1-methyl-2 pyrrolidinone led us also to explore the biological implications of the formation of the amide peroxide. Comparison to the amino-acid proline in cytochrome P-450, a naturally occurring oxidant, suggested that the formation of a peroxide from the substituted pyrrolidine ring of the proline in cytochrome P-450 may provide an alternate pathway for the oxidation of organic substrates by cytochrome P-450.

In addition to the discovery of the 1-methyl-5-peroxy-2 pyrrolidinone, the ability of the peroxide to epoxidize alkenes and to oxidize alkanes and alkyl sulfides is investigated. The epoxidation of alkenes by the peroxide provides support for our belief that the formation of a peroxide of the proline contained in cytochrome P-450 is capable of providing an alternative mechanism for the oxidation of alkenes. The possibility of forming chiral epoxides from 5-substituted pyrrolidinones (1,5-dimethyl-2-pyrrolidinone) is also touched upon and shows that it should be quite possible to form chiral peroxides from chiral 5-substituted 1-methyl-2-pyrrolidinone.

CHAPTER 2
OXIDATION OF 1-METHYL-2-PYRROLIDINONE

Background

The oxidation of tertiary alkylamines to amine oxides by molecular oxygen[1,2] and hydrogen peroxide[3,4] is well known and has been documented in the literature. The oxidation of amides to imides by hydrogen peroxide[5], persulfates[6], and molecular oxygen[7,8,9] has also been succesfully demonstrated both with and without the use of transition metal catalysts. In the process of oxidizing amides to their imides, a hydroperoxide intermediate can be isolated from the mixture. The utilization of tertiary alkylamine oxides has been reported in the literature as a process for selectively oxidizing alkenes to their epoxides[10,11] and diols.[12,13] In this research we shall consider both these reactions for the selective oxidation of alkenes to their epoxides.

The synthesis of amine oxides from tertiary amines with hydrogen peroxide is believed to proceed by a mechanism involving a peroxide intermediate which decomposes to the amine oxide. Infrared spectroscopy experiments by Oswald and Guertin[14] at -50°C found that the tertiary amine-hydrogen peroxide adduct is a hydrogen bonded polar complex and not an ionic ammonium salt.

$$R_3N \ldots H\text{-}O\text{-}O\text{-}H \qquad (1)$$

Oswald and Guertin proposed the following equation for the decomposition of

the tertiary amine-hydroperoxide adduct to the amine oxide.

$$R_3N \cdot H_2O_2 \dashrightarrow R_3NO \cdot H_2O \qquad (2)$$

The decomposition of the amine-hydrogen peroxide adduct to the amine oxide was highly exothermic and gave greater than ninety percent yield of amine oxide.[14]

In the reaction of tertiary alkyl amines with alkyl hydroperoxides, the addition of transition metal complexes greatly enhanced the yield of amine oxide relative to the amount of alkyl hydroperoxide consumed in the reaction.[3] The addition of molybdenum, vanadium and tungsten complexes increased the product yield two- or three-fold relative to the quantity of amine oxide produced without transition metal complexes present.

On the other hand, the addition of cobalt, manganese, and iron catalysts rapidly decomposed the alky hydroperoxide to its corresponding alcohol, while giving yields of amine oxide from one-tenth to one-third that of the blank. The group VIIB and VIIIB transition metal complexes rapidly decomposed the alkyl hydroperoxides without promoting the oxidation of the tertiary amines, while the molybdenum, tungsten and vanadium complexes must have formed metal peroxides which oxidized the tertiary amines to their amine oxides.

The oxidation of tertiary amines to amine oxides by molecular oxygen in water is believed to proceed by two different mechanisms affected by the O_2 pressure and the temperature of the reaction.[1] The low pressure pathway involves the formation of hydrogen peroxide and amine hydroperoxides, which are derived from alpha-oxidation by reaction with a free-radical initiator or an electron acceptor. These peroxides react with the tertiary amine to form amine oxides in a mechanism similar to those described earlier.[15]

The high yields of product (greater than 50%), derived from the reaction of tertiary amines with molecular oxygen in water at increased oxygen pressures (71-86 bar) and elevated temperatures (100-116°C), indicate that the mechanism of oxidation was fundamentally different from the peroxide mechanism proposed by Beckwith[15] and that a new mechanism, involving molecular oxygen, was necessary to explain the product yields. Riley and Correa[1] proposed that the reaction involved an initial electron transfer, yielding an amine radical cation and superoxide (eq. 3). This reaction was the rate limiting step in a chain reaction which produced amine oxides.

$$NR_3 + O_2 \rightleftharpoons R_3N^{+\cdot} + O_2^{-\cdot} \tag{3}$$

This explained why the reaction was first-order in both tertiary amine and molecular oxygen. It also explained the slow rate of reaction, since the electron transfer is endothermic.[1] The high oxygen concentration was believed to permit the interception of the solvent-stabilized amine radical cation before it was deprotonated at the alpha-CH (eq. 4). The reduction of the hydroperoxy radical cation was proposed to be done by either another tertiary amine (eq. 5) or by superoxide (eq. 6). The zwitterion produced by these reactions reacted with a tertiary amine to produce the amine-oxide product (eq. 7).

$$R_3N^{+\cdot} + {}^3O_2 \rightleftharpoons R_3N^+OO^\cdot \tag{4}$$

$$R_3N^+OO^\cdot + R_3N \rightleftharpoons R_3N^+OO^- + R_3N^{+\cdot} \tag{5}$$

$$R_3N^+OO^\cdot + O_2^{-\cdot} \rightleftharpoons R_3N^+OO^- + O_2 \tag{6}$$

$$R_3N^+OO^- + R_3N \rightleftharpoons 2 R_3NO \tag{7}$$
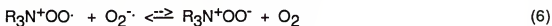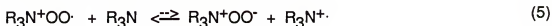
The autoxidation of amines to amine hydroperoxides is strongly dependent on the reaction solvent. In polar solvents, such as water, the reaction is not greatly effected by radical initiators or inhibitors. The reaction is instead, sensitive to the addition of electron acceptors such as benzoquinone[15] or methylene blue.[16] The reaction is initiated predominantly by electron transfer, producing the aminium radical cation (equation 8) which is an effective protic acid and is converted into the radical following the loss of a proton (equation 9). The radical then reacts with molecular oxygen to form the peroxy radical (equation 10) or the iminium ion (equation 11). The iminium ion reacts with water to form the amino alcohol and the amide (equation 12).[15]

$$\underset{R}{N} + A \longrightarrow \underset{R}{\overset{+}{N}}{\cdot} + A^{-\cdot} \tag{8}$$

$$\underset{R}{\overset{+}{N}}{\cdot} + B \longrightarrow \underset{R}{N}{\cdot} + BH \tag{9}$$

$$\underset{R}{N}{\cdot} + O_2 \longrightarrow \underset{R}{N}O_2{\cdot} \tag{10}$$

$$\underset{R}{N}{\cdot} + O_2 \longrightarrow \underset{R}{\overset{+}{N}} + O_2^{-\cdot} \tag{11}$$

$$\underset{R}{\overset{+}{N}} + H_2O \longrightarrow \underset{R}{N}OH + \underset{R}{N}{=}O \tag{12}$$
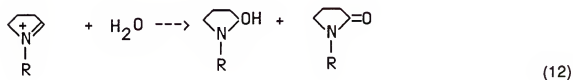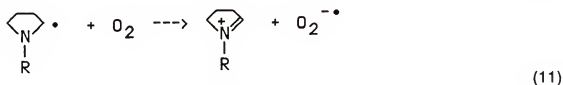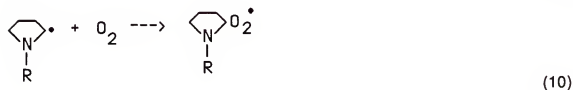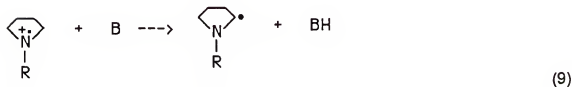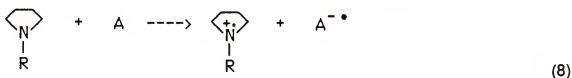
In nonpolar solvents, the autoxidation of amines is enhanced by the presence of initiators and can be diminished by inhibitors. It is proposed that this reaction will occur by means of a free-radical mechanism in which an initiator reacts with the amine to form a radical (eq. 13), which in turn reacts with molecular oxygen to form a peroxide radical (eq. 14). The peroxide radical abstracts a hydrogen atom from the alpha-carbon of a second amine to form the peroxide and another radical (eq. 15). Reactions 14 and 15 are chain propagating steps in the free-radical autoxidation of amines to their peroxides. The last step in the reaction is the chain-terminating reaction (eq.16) in which only oxygenated radicals are involved.[15]

$$\langle N R \rangle \quad + \quad In\cdot \quad \longrightarrow \quad \langle N R \rangle \cdot \tag{13}$$

$$\langle N R \rangle \cdot \quad + \quad O_2 \quad \longrightarrow \quad \langle N R \rangle O_2 \cdot \tag{14}$$

$$\langle N R \rangle O_2 \cdot \; + \; \langle N R \rangle \quad \longrightarrow \quad \langle N R \rangle O_2 H \; + \; \langle N R \rangle \cdot \tag{15}$$

$$2 \; \langle N R \rangle O_2 \cdot \quad \longrightarrow \quad molecular\ products \tag{16}$$
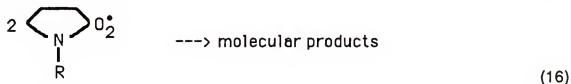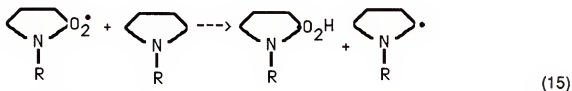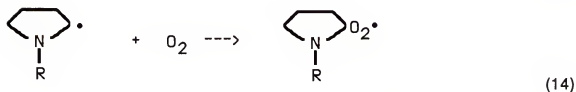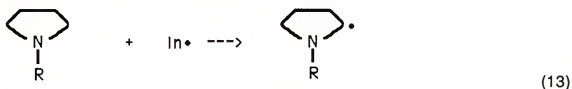
The formation of the amide probably occurs by decomposition of the peroxide in nonpolar solvents or the neat substrate (eq.17).

(17)
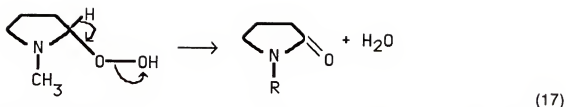
The major product of the autoxidation of N-methylpyrrolidine is, however, the amine oxide which arises from oxidation by hydrogen peroxide and the amine hydroperoxide in aqueous solution. Separate experiments have shown that N-methylpyrrolidine is rapidly converted to the amine oxide by treatment with hydrogen peroxide.[15] For the oxidation of amides, this reaction does not occur and only the products arising from the formation of the amine hydroperoxide are observed.

Oxidation of the amides to their imides has been reported in the literature for the straight chain alkyl amides[5] and the 5- and 6-membered lactams.[5,6] A similar oxidation pathway has been found for alkenes[17] and ethers[18] in which a hydrogen is abstracted from a carbon that is adjacent to the double bond of the alkene or the oxygen of the ether. The abstraction of a hydrogen atom from a carbon adjacent to a nitrogen in an amine has a rate constant much higher, however, than those of alkenes and isostructural ethers. Oxygen attack on the methylene group adjacent to the amide nitrogen is also reported for the photooxidation of N-alkyamides.[19] The oxidation of the straight chain alkylamides is characterized by autoxidation at the primary carbon of the hydrocarbon chain. The carbon atoms in the ketone chain are not effected. In the case of the 5 and 6-membered lactams, the oxidation takes place at positions 5 and 6 in 5 and 6-membered rings, respectively.

R-CH-NH-C-R * N CH$_3$ O * N R O
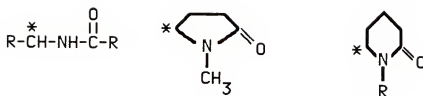
The autoxidation of amides proceeds by a peroxy-radical mechanism very similar to that of the amines; however, the oxidation of amides to their amine oxides did not occur. The most common oxidation which occurred during this reaction was that of the amide to the imide.[5,6] Attempts to oxidize 5 and 6 membered lactams with persulfates to their ring-opened products, the w-aldehydoamides, yielded imides as the primary products (23-61%). The oxidation of 1-methyl-2-pyrrolidinone with persulfate yielded 35% N-methylsuccinimide.[6]

Large quantities of the imides were also produced in the presence of transition-metal ions such as Co(II), Mn(II) or Mn(III)[5,20] by alkyl hydroperoxides and peracetic acid. The oxidations of 2-pyrrolidinone and 1-methyl-2 pyrrolidinone produced their respective imides: succinimide (90% yield) and N-methylsuccinimide (55% yield) when oxidized in ethyl acetate.[5]

The oxidation of amides to imides has also been performed electrochemically in acetonitrile in excellent yield.[21,22] The electrochemical oxidations also produced the alpha-alcohol of the amide during this reaction.[21]

The autoxidation of amides by molecular oxygen has been demonstrated to yield both the imides and the hydroperoxides. The catalytic oxidation by KMnO$_4$ with O$_2$ of 1-methyl-2-pyrrolidinone to N-methylsuccinimide has been performed successfully.[23] The autoxidation of N-alkylamides with molecular oxygen gave three principal products: formation of N-acylamides(eq. 18),

formation of N-formylamides as a result of C_1-C_2 bond scission(eq. 19) and
oxidative dealkylation to yield carbonyl compounds (eq. 20).[7]

$$R\text{-CO-NH-CH}_2R' \longrightarrow R\text{-CO-NH-CO-R'} \qquad (18)$$

$$R\text{-CO-NH-CH}_2R' \longrightarrow R\text{-CO-NH-CO} \qquad (19)$$

$$R\text{-CO-NH-CH}_2R' \longrightarrow RCONH_2 + R'CHO \qquad (20)$$

For the autoxidation of a tertiary amine such as 1-ethyl-2-pyrrolidine at $131^{O}C$,
the principal stable products were 1-acetyl-2-pyrrolidine(A), 2-pyrrolidinone(B)
and 1-ethylsuccinimide(C) which are displayed in equation 21.

N–Ac	N–H	N–Et
(A)	(B)	(C)
8.1%	21%	71%

$$(21)$$
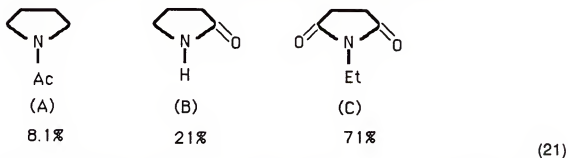
This experiment demonstrates that attack on the alpha-carbon of the ring is 2-3
times more probable than attack on the exocyclic N-ethyl group.[7] The formation
of (A) and (C) can be explained by reaction 17 as they are N-acylamide
products. Product (B) is the result of an oxidative dealkylation (eq. 19) which
forms acetaldehyde and 2-pyrrolidinone. The formation of these three products
can be explained by a peroxy-radical mechanism[7,9] in which a hydrogen atom
is abstracted from a carbon adjacent to the nitrogen by an initiator such as a
1-amidoalkoxy-radical, which is formed by the breakdown of amide
hydroperoxide during thermal oxidation or by an added radical initiator. The
free-radical initiators used for these experiments were t-butyl hydroperoxide,

benzoyl hydroperoxide and alpha alpha'-azodi-isobutyronitrile(AIBN).[8,9] The mechanism proposed for the thermal oxidation of amides, initiated by AIBN, follows the same mechanism as that proposed for the amine oxidations described by Beckwith.[15] In Beckwith's mechanism, the radical formed by decomposition of the AIBN ($R^{2\cdot} = Me_2\overset{\cdot}{C}CN$) reacts with molecular oxygen to form $R^2O_2\cdot$ which in turn initiates reaction 8 and begins the chain reaction to form the alpha-peroxide of the amide.[9] Once the reaction has begun, radical initiators and transition metal catalysts such as Cu(II), Fe(III) and Co(II) in low concentrations (1-2.5ppm) failed to increase the maximum concentration of peroxide products, while high concentrations (50ppm) of Co(II) greatly decreased the maximum concentration of hydroperoxides.[8] The negative effect of high concentrations of Co(II) on high peroxide concentration is presumably due to the accelerated decomposition of the hydroperoxides by the Co(II), which is an efficient peroxide decomposition catalyst.

From the evidence shown above, it can be inferred that the thermal oxidation of the amides proceeds by means of a peroxy-radical chain mechanism. Both the hydroperoxides and the other products observed in the thermal oxidation of amides can be explained in terms of the peroxy-radical mechanism and the subsequent heterolytic decomposition of the peroxides produced during that reaction.[8]

Materials

The 1-methyl-2-pyrrolidinone was hplc grade from Aldrich and was used as received. The 1,5-dimethyl-2-pyrrolidinone was also from Aldrich and was

vacuum distilled prior to use. The 2-pyrrolidinone and L-prolinamide were purchased from Aldrich and used as received. The Co(octoate)$_2$ (octoate = 2-ethylhexanoate) catalyst was an oil solution that was 12% cobalt(II) by weight. This catalyst was purchased from Mooney and was used as received.

Methods

Electronic and vibrational spectroscopy were performed as described previously. Proton and ^{13}C nmr spectroscopy were run on a Varian XL-300 instrument in deuterated benzene or chloroform with TMS as an internal standard in all samples. The ^{13}C nmr assignments were made using the Attached Proton Test (APT)[24,25,26] and the Distortionless Enhancement by Polarization Transfer (DEPT)[27] programs available on the Varian XL-300.

GC-MS were performed on a Finnigan 700 Ion Trap Detection System(ITDS) with a Varian 3400 GC containing a 15m SPB-1 capillary column and by the University of Florida Microanalytical Labs on a Finnigan single quadrupole mass spectrometer connected to a Hewlett-Packard 5890A GC containing a direct on-column injector into a 30m DB-1 column. Chemical ionization with methane was used to detect the parent ion of the peroxide because the molecular ion of the peroxide was not formed during normal ionization.

The oxidations under 50 psig O$_2$ pressure were performed in a 250ml Parr pressure apparatus (see figure 2-1) which was sampled by syringe (12 inch, 20 gauge needle).

All reactions were performed at 75°C under 50 psig oxygen unless stated otherwise. The substrate was used as the solvent for the oxidation of 1-methyl-2-pyrrolidinone and 1,5-dimethyl-2-pyrrolidinone.

For the oxidation of L-prolinamide and the acylated L-prolinamide, acetonitrile was used as the solvent. Vacuum distillation of the 1-methyl-2 pyrrolidinone from the peroxide was performed with an oil diffusion pump at 0.0001mbar and approximately 30 to 40°C.

Peroxide concentrations were measured by taking 0.5-2ml samples from the pressure bottles with a 12 inch stainless steel needle and immediately iodometrically titrating them by the Sharpless method.[28] The 0.1N $Na_2S_2O_3$ solution was made with standard solutions purchased from Aculute.

The reduction of N-methylsuccinimide was carried out under 55 psig hydrogen in the Parr pressure bottle shown in figure 2-1. The N-methylsuccinimide and 1-methyl-2-pyrrolidinone were separated on a Varian 3700 GC using a six foot stainless steel 15% FFAP(ChromW,A/W 80/100 mesh support) column and integrated on a Hewlett-Packard 3390A integrator.

The acylation of L-prolinamide was performed by an adapted literature method.[29] L-prolinamide (1.5g), acetyl chloride (1.31g), triethylamine (1.55g) and 100ml of methylene chloride were stirred overnight at room temperature in a 250ml roundbottom flask.

Prior to the addition of acetyl chloride, the solution was briefly purged with nitrogen to remove water and then tightly stoppered for the duration of the reaction. The next morning the solution was rotovapped at room temperature and filtered to remove the reacted triethylamine as Et_3NHCl.
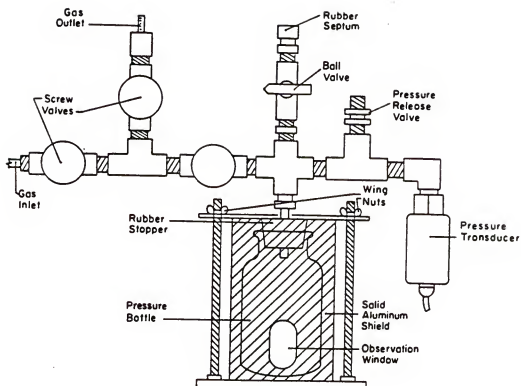
Figure 2-1   Parr pressure bottle setup for oxidation of
toluene by molecular oxygen.

0.5g L-prolinamide and approximately 1g of the acylated prolinamide were dissolved in 25ml aliquots of acetonitrile and placed in Parr pressure bottles under 50 psig oxygen according to methods described earlier.

Results and Discussion

The oxidation of 1-hexene by CoCNY in mp gave very encouraging results as seen in figure 2-2. The major product of the reaction was 1,2-epoxyhexane. The tremendous increase in the selectivity for the desired product, the epoxide, suggests that a different type of reaction was taking place in 1-methyl-2 pyrrolidinone. The same reaction in acetonitrile almost exclusively produced the 1-hexen-3-ol and 1-hexen-3-one.

In order to determine exactly which oxidizing species are present in the oxidation of alkenes by molecular oxygen in 1-methyl-2-pyrrolidinone, we performed a series of experiments in which we ascertained that 1-methyl-2 pyrrolidinone was oxidized under reaction conditions. Titration by the Sharpless method[28] showed that the oxidation of the neat 1-methyl-2 pyrrolidinone (figure 2-3) at 75°C under 50 psig molecular oxygen produced a large quantity of an oxidizing species. We believe that these oxidants were active in the oxidation of alkenes in 1-methyl-2-pyrrolidinone. By contrast, under the same conditions, 2-pyrrolidinone did not generate an oxidizing species and was incapable of oxidizing alkenes under these conditions. Under the same conditions, N-methylmorpholine also failed to generate an oxidizing species, despite the fact that it is known to generate the N-oxide at higher
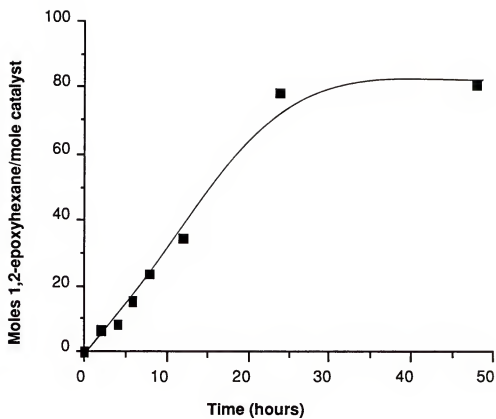
Figure 2-2 Catalytic oxidation of 1-hexene in 1-methyl-2
pyrrolidinone by p77-270 CoCNY catalyst.
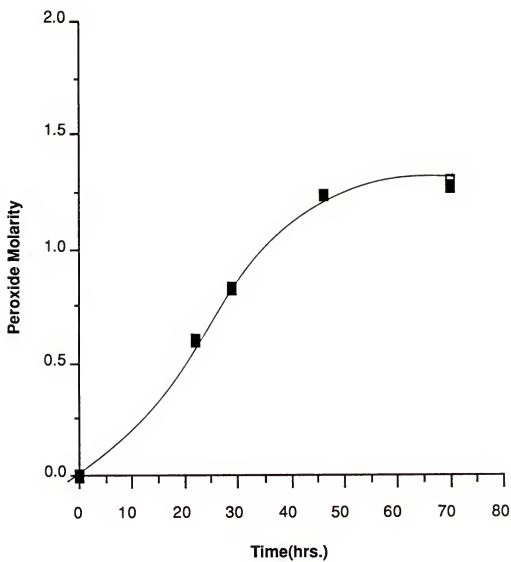
Figure 2-3 Oxidation of 1-methyl-2-pyrrolidinone at 75 C
under 50 psig oxygen without catalyst.

temperatures and pressures.[1] Instead of forming the N-oxide at 75°C, the N-methylmorpholine was polymerized to a brown solid.

Triphenylphosphine Oxidation

In addition to the preliminary identification of an oxidizing species, experiments were performed to determine the efficiency of the reaction and whether or not this oxide was potentially a good oxidant. An experiment was performed to measure the quantity of oxygen required to produce one mole of oxidant in 1-methyl-2-pyrrolidinone at 75°C under 50 psig oxygen, thereby determining the efficiency of the reaction between molecular oxygen and 1-methyl-2-pyrrolidinone. This was done by measuring the volume of the vessel(270ml - 50ml 1-methyl-2-pyrrolidinone = 220ml) and calculating the number of moles of oxygen in it using the equation PV=nRT to give 0.0262 moles of oxygen. When all of the oxygen had been consumed (1-methyl-2 pyrrolidinone is not volatile at 75°C. Therefore, all of the oxygen had been consumed when the pressure in the vessel equaled zero.), the oxidized 1-methyl-2-pyrrolidinone was titrated to measure the quantity of oxidant present. The results of this experiment indicate that a ratio of 1.5 moles of dioxygen were consumed to form 1 mole of the oxidizing species. The rest of the oxygen was presumably dissolved or consumed in the formation of N-methylsuccinimide. When this same solution of 1-methyl-2-pyrrolidinone oxidant was deoxygenated with argon and placed in an oil bath at 75°C with triphenyl phosphine, triphenyl phosphine was oxidized to triphenyl phosphine oxide in a ratio of 2.7 moles of oxidant to one mole of triphenyl phosphine oxide. This was measured by calculating the area of the triphenyl phosphine oxide P=O stretching frequency

at 722cm^{-1} in the IR (as seen in figure 1-4) by cutting and weighing both the sample and standards. In figure 2-5 one can see that there is no interference with this band from either triphenyl phosphine or 1-methyl-2-pyrrolidinone and in figure 1-6 one can also see that, although the oxidized 1-methyl-2 pyrrolidinone has new bands at 760cm^{-1} and 790cm^{-1}, they are well above the band at 722cm^{-1} and did not interfere with the measurement of the peak's area. This evidence proves that an oxidizing species can be produced through oxidation of 1-methyl-2-pyrrolidinone with molecular oxygen and that this species is capable of oxidizing triphenyl phosphine to triphenyl phosphine oxide.

The first experiment determined which oxidizing species were present using CoBPI (Mimoun's peroxide decomposition catalyst[30]) to oxidize 1-methyl-2 pyrrolidinone to the peroxide at 75°C. In the first 24 hours of reaction, virtually no oxidant was present in the solution as measured by iodine titration (figure 2-7). We did observe a large amount of N-methylsuccinimide formed in this time period as measured by gas chromatography. After 24 hours of reaction time, the solution decolorized, indicating that the CoBPI had decomposed and from then on the iodine titrations indicated that the oxidizing species was present in the solution in increasing quantities. Since CoBPI is a peroxide decomposition catalyst, the evidence of this experiment leads one to believe that the titrated oxidant is a 5-peroxide of 1-methyl-2-pyrrolidinone and that it was decomposed by the CoBPI to N-methylsuccinimide. The 5-peroxide may have been formed by a mechanism very similar to that discussed earlier for the formation of 1-methyl-2-peroxypyrrolidine in equations 13 through 16.
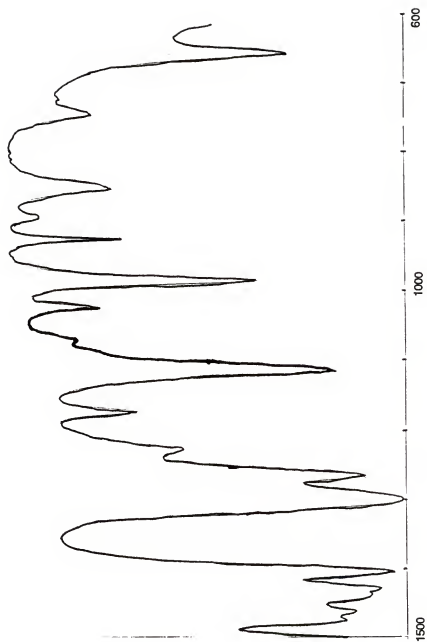
Figure 2-4   IR of triphenyl phosphine oxide dissolved in
1-methyl-2-pyrrolidinone
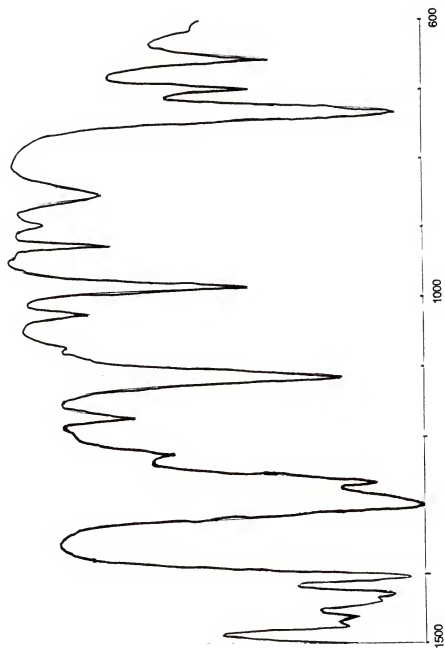
Figure 2-5   IR of triphenyl phosphine in 1-methyl-2
pyrrolidinone after 24 hours at 50°C under
argon.
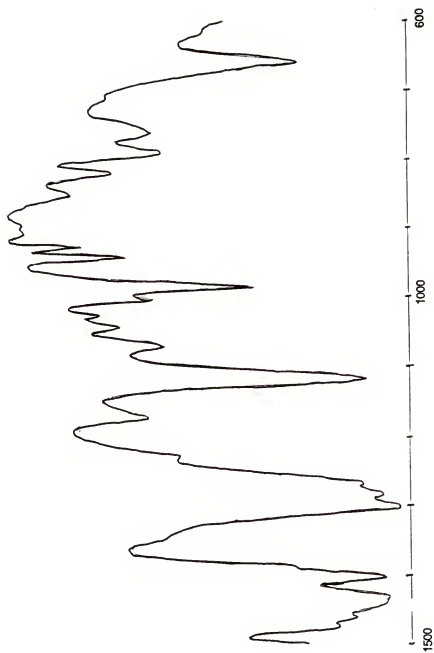
Figure 2-6   IR of 1-methyl-2-pyrrolidinone after oxidation at 75°C under 50 psig oxygen.
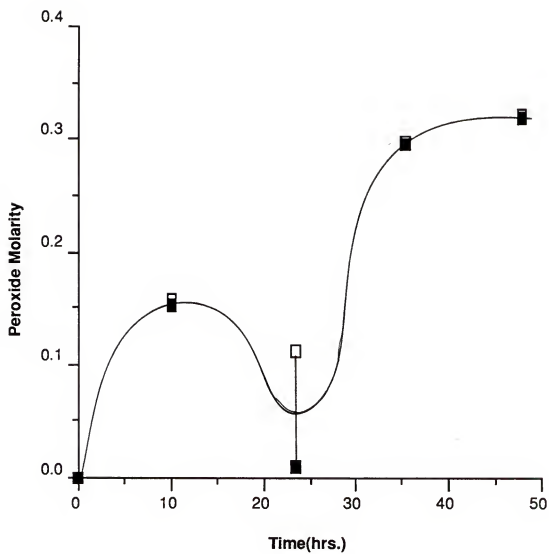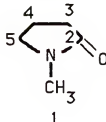
Figure 2-7 Oxidation of 1-methyl-2-pyrrolidinone by CoBPI
at 75 C with 50 psig oxygen.

<u>NMR data</u>

To determine whether or not this oxidant was the 5-peroxide, we used ^{13}C and proton NMR in our attempts to identify the oxidizing species present in 1-methyl-2-pyrrolidinone after oxidation at 75°C under 50 psig oxygen. The proton spectrum of 1-methyl-2-pyrrolidinone (figure 2-8) contained two triplets centered at 2.96 and 2.06ppm, a quintuplet centered at 1.61ppm and a singlet at 2.61ppm. The ^{13}C nmr spectrum of 1-methyl-2-pyrrolidinone (figure 2-9) had peaks at 174.4, 49.4, 30.9, 29.4 and 18.3ppm. The ^{13}C peaks were assigned using both the distortionless enhancement by polarization transfer (DEPT) and the attached proton test (APT) (figure 2-10) programs on the XL-300 nmr. Our peak assignments were in agreement with those reported in the literature.[31] The ^{13}C peak assignments are shown in table 2-1.

Table 2-1
DEPT and APT assignment of ^{13}C nmr for 1-methyl-2-pyrrolidinone

Carbon	13C nmr peak(ppm)
1	29.3
2	174.3
3	30.8
4	18.2
5	49.4

The carbon-hydrogen correlation was assigned by the HETCOR program available on the Varian XL-300 using 2-dimensional nmr (figure 2-11) and gave the following assignments. Having made these assignments, we could follow the changes in the nmr of the neat substrate during its oxidation.
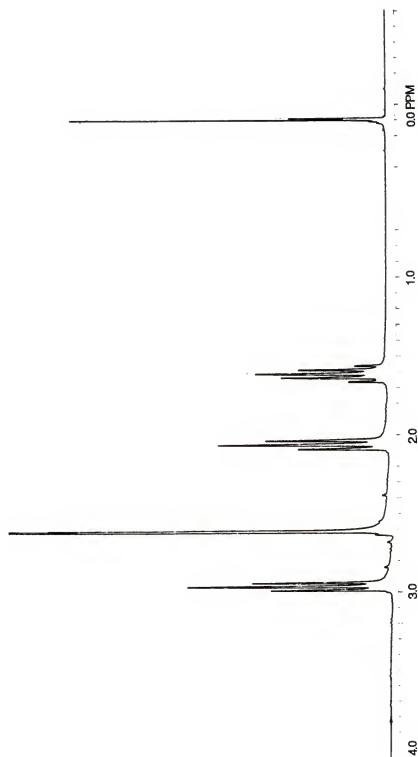
Figure 2-8   Proton nmr of 1-methyl-2-pyrrolidinone (in C_6D_6, TMS).
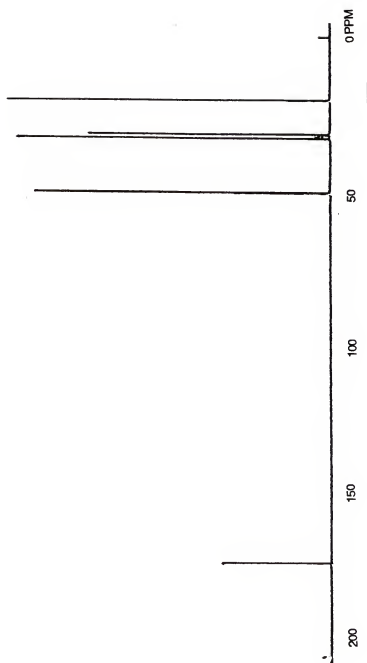
Figure 2-9   13C nmr of 1-methyl-2-pyrrolidinone
(in CDCl$_3$, TMS).
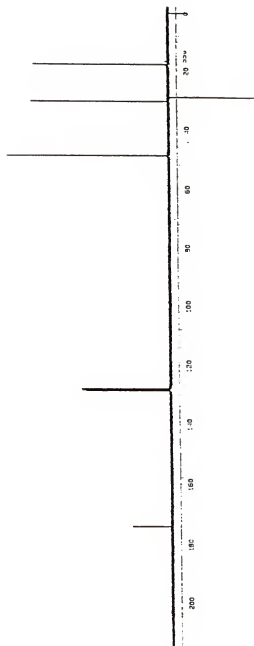
Figure 2-10   APT ^{13}C nmr of 1-methyl-2-pyrrolidinone (in C_6D_6, TMS).
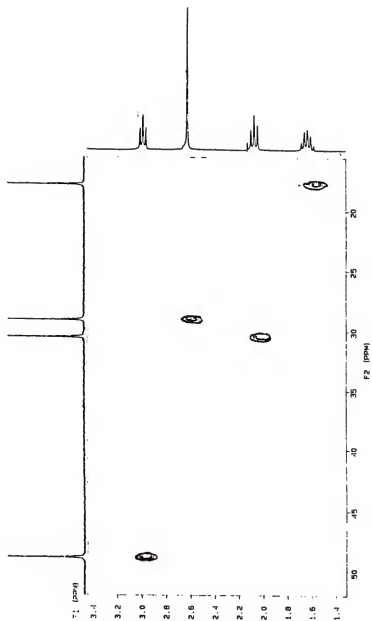
Figure 2-11   Proton/Carbon 2-D correlation nmr of
1-methyl-2-pyrrolidinone (in C_6D_6).
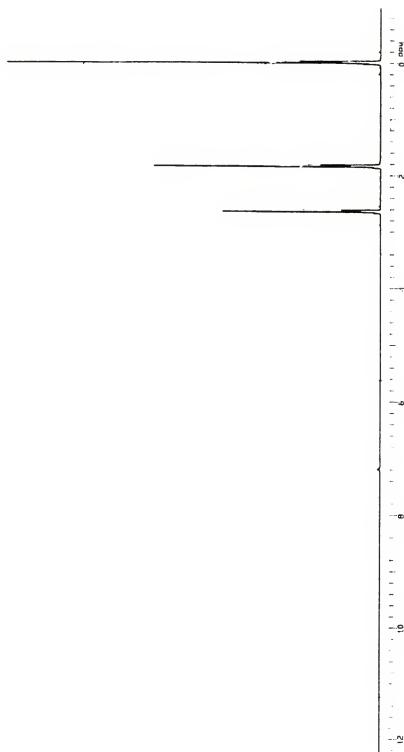
Figure 2-12 Proton nmr of N-methylsuccinimide(in C6D6, TMS).
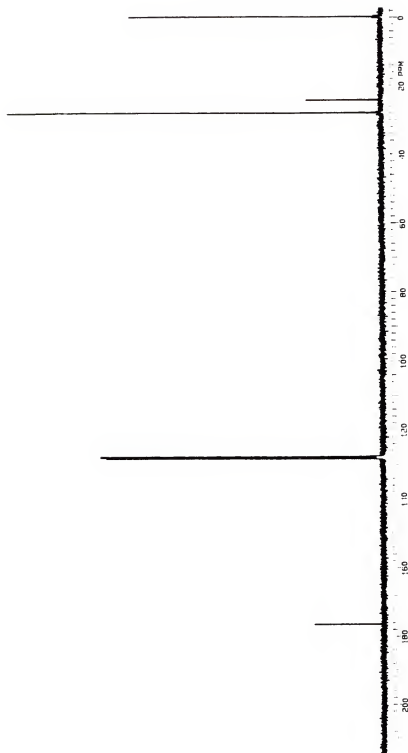
Figure 2-13   13C nmr of N-methylsuccinimide(in C6D6, TMS).

We were also able to assign the ^{13}C (figure 2-12) and proton (figure 2-13)nmr peaks for N-methylsuccinimide by the same method. 2-dimensional nmr (figure 2-14) and APT (figure 2-15) were used to assign the following N-methylsuccinimide peaks.

Table 2-2
Proton/Carbon 2-d correlation assignments for 1-methyl-2-pyrrolidinone
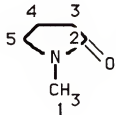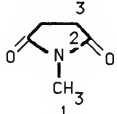
Carbon	^{13}C (ppm)	^{1}H (ppm)
1	29.3	2.61 singlet
2	174.3	
3	30.8	2.06 triplet
4	18.2	1.61 quintuplet
5	49.4	2.96 triplet

Table 2-3
DEPT and Proton/Carbon 2-d correlation assignments for N-methylsuccinimide

Carbon	C(ppm)	H(ppm)
1	24.1	2.64 singlet
2	176.2	
3	27.8	1.84 singlet

By assigning the spectrum of 1-methyl-2-pyrrolidinone and N-methylsuccinimide, all other species present were distinguished from the original starting material and the inactive (non-oxidant) N-methylsuccinimide.

By following the oxidation of the neat 1-methyl-2-pyrrolidinone at 75°C under 50 psig oxygen over a period of 48 hours, the formation of a new species
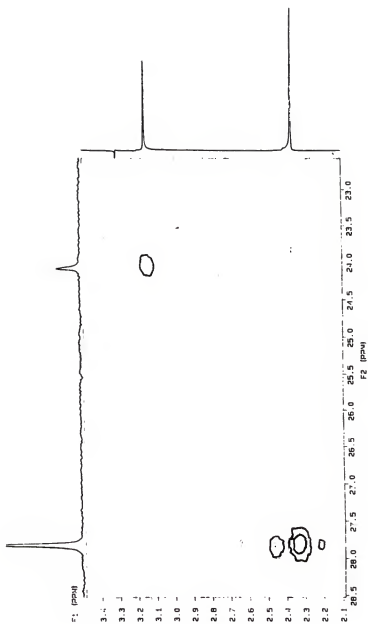
Figure 2-14 Proton/Carbon 2-D correlation nmr of N-methylsuccinimide(in C6D6).
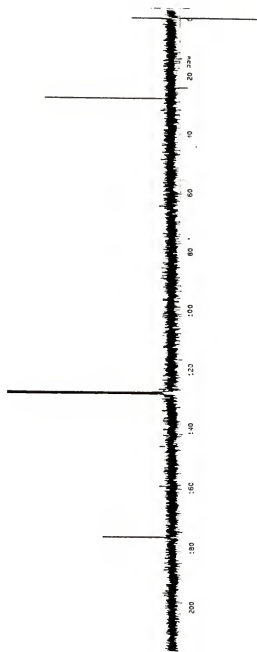
Figure 2-15   APT 13C nmr of N-methylsuccinimide(in C6D6).

was observed which we believe to be the 1-methyl-5-peroxy-2-pyrrolidinone. This was an appropriate intermediate in the oxidation of 1-methyl-2 pyrrolidinone to N-methylsuccinimide and would fit in well with the mechanisms for the oxidation of amides, described previously in equations 13-16.

The ^{13}C nmr spectrum in figure 2-16, taken from a sample that had been oxidized for 13.5 hours (at 75°C under 50 psig oxygen), contains five new peaks at 174.9, 94.6, 29.8, 27.3 and 23.7ppm, which would imply that a new species was present in the solution and was most likely an oxidation product of the 1-methyl-2-pyrrolidinone, rather than an indication that a polymer of 1-methyl-2-pyrrolidinone was forming. The nmr spectrum contained five new peaks, which would be consistent with a 1-methyl-5-peroxy-2-pyrrolidinone species in solution. The iodine titration data revealed the presence of a peroxide, giving further support to this hypothesis. In addition, the formation of a polymer would most likely have produced a product containing fewer nmr peaks than did our starting material. A polymer such as the one shown below would have only three ^{13}C nmr peaks, not five.
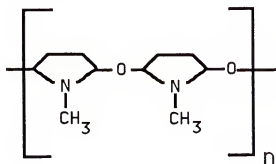
The integration of the nmr in figure 2-17 shows that all five peaks are of the same size. This implies that they all belong to the same molecule.
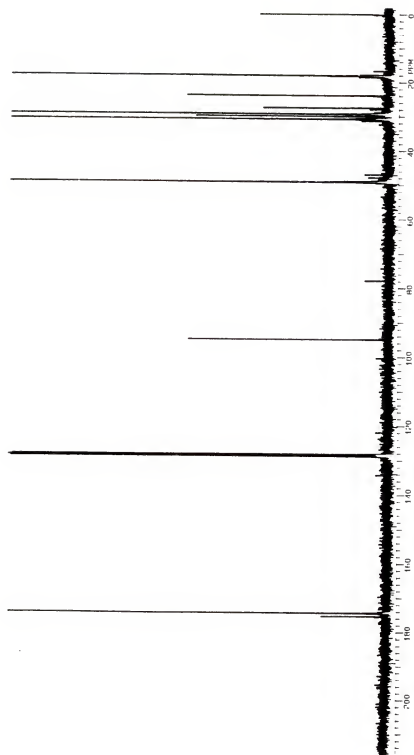
Figure 2-16   13C nmr of 1-methyl-2-pyrrolidinone oxidized for
                13.5 hours at 75oC under 50 psig oxygen
                (in C6D6, TMS).
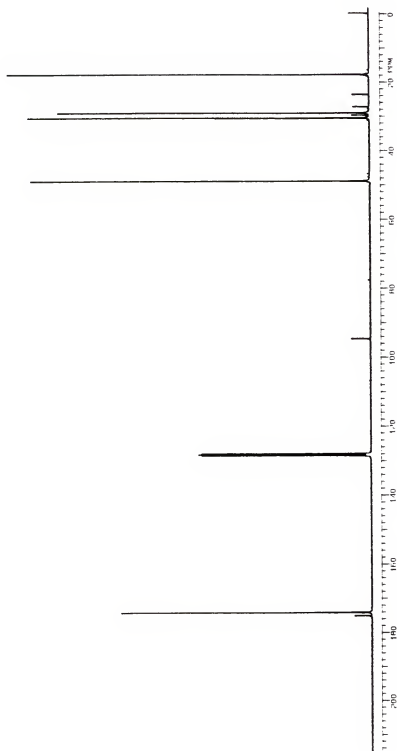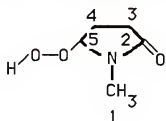
Figure 2-17   Quantitative 13C nmr of 1-methyl-2-pyrrolidinone
              oxidized for 13.5 hours at 75oC under 50 psig
              oxygen (in C6D6, TMS).

It was determined by the DEPT program that the peaks at 23.7 and 29.8ppm were CH_2 carbons, the peak at 27.3ppm was for a CH_3 carbon, the peak at 175.1ppm was for a carbon which had no attached protons and the peak at 94.7ppm was for a carbon with a single proton attached to it. The peak assignments were made for a 1-methyl-5-peroxy-2-pyrrolidinone as follows in table 2-4. These peak assignments correlate with those of a peroxide. In an experiment with cumene hydroperoxide, the nmr spectra of the cumene, cumenen hydroperoxide and cumyl alcohol and acetophenone, were obtained for comparison to those obtained for 1-methyl-2-pyrrolidinone, N-methylsuccinimide and 1-methyl-5-peroxy-2-pyrrolidinone.

Table 2-4
DEPT ^{13}C assignments for 1-methyl-5-peroxy-2-pyrrolidinone

Carbon	C(ppm)
1	27.3
2	175.1
3	29.8
4	23.7
5	94.7
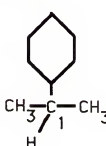
The ^{13}C and proton nmr spectrum of the cumene compounds were obtained and compared to those of the 1-methyl-2-pyrrolidinone products.

This data revealed a shift of 57.4ppm from cumene to the cumene hydroperoxide for carbon 1. There is also a shift of 38ppm from cumene to the cumyl alcohol for carbon 1. For the change from cumene to cumene hydroperoxide, the large shift from C-H to COOH corresponds to the 45.3ppm

shift observed in carbon 5 of 1-methyl-2-pyrrolidinone to the 1-methyl-5
peroxy-2-pyrrolidinone.

The proton nmr data was decidedly ambiguous for the oxidized
1-methyl-2-pyrrolidinone. In figures 2-18 and 2-19, two new peaks were

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Table 2-5
^{13}C nmr data for cumene oxide

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Type		^{13}C nmr for carbon 1(ppm)
cumene	C–H	26.3
cumene hydroperoxide	COOH	83.7
cumyl alcohol	C–OH	64.3
acetophenone	C=O	197

observed in the nmr that were not due to 1-methyl-2-pyrrolidinone or
N-methylsuccinimide. The triplet centered at 2.82ppm was small after 24 hours,
but was a very large singlet after 48 hours (figure 2-19), while the multiplet at
2.4ppm did not change in that time period. The oxidized
1-methyl-2-pyrrolidinone was distilled in order to concentrate the peroxide, but
this did not concentrate the solution enough for the 2-dimensional nmr to
correlate the peak at 2.82ppm with a peak in the ^{13}C spectrum of the peroxide.
The very small triplet centered at 5.2ppm and the singlet at 5.0ppm in figure
2-19 were also unidentifiable through 2-dimensional nmr. The peak at 2.82ppm
was possibly due to an interaction between a peroxide oxygen atom and one of
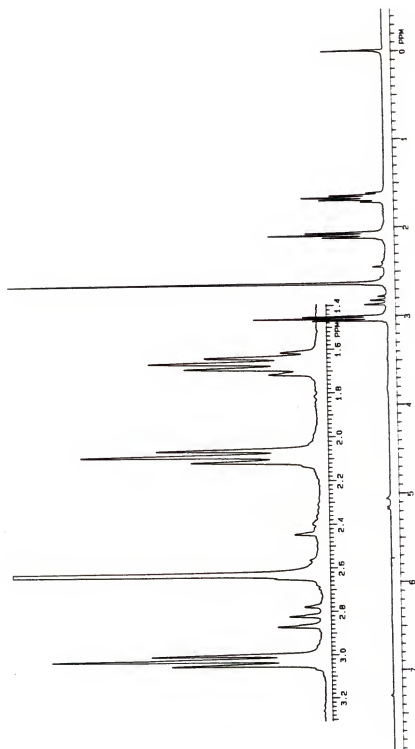
Figure 2-18   Proton nmr of 1-methyl-2-pyrrolidinone oxidized for
24 hours at 75oC under 50 psig oxygen(in C6D6, TMS).
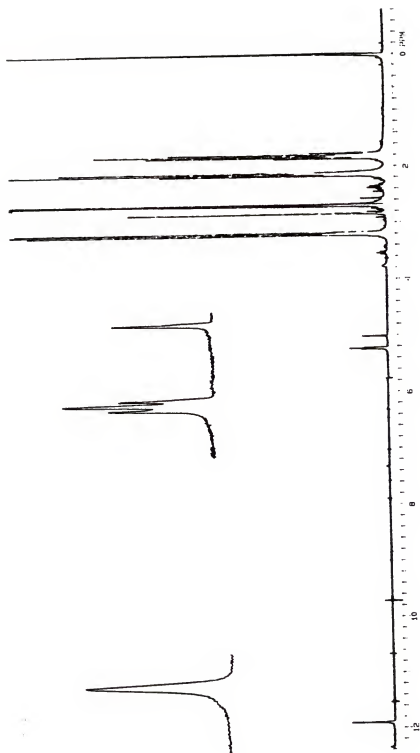
Figure 2-19   Proton nmr of 1-methyl-2-pyrrolidinone oxidized for
48 hours at 750C under 50 psig oxygen(in C6D6, TMS).

the protons attached to carbon 1, but without support from either 2-dimensional nmr or another technique, it is impossible to make definite assignments for the new peaks appearing at 2.82, 5.0, and 5.2ppm in figure 2-19.

Figures 2-16, 2-20, 2-21 and 2-22 are ^{13}C nmr spectra of oxidation reaction samples taken at 13.5, 36, 48 and 48 hours respectively. The oxidation of the neat substrate without catalyst at 75°C gives the peroxide almost exclusively in all four nmr. Figures 2-21 and 2-22 contain small peaks indicating the presence of another oxidized product which was not the N-methylsuccinimide. The peaks were at 77.6, 46.8, 31.2, 28.6 and 18.3ppm and were all approximately the same size. Since this new species has five nmr peaks, the basic structure of the pyrrolidine ring must be intact. This product is not 2-pyrrolidinone, the oxidative dealkylation product that is observed by Sagar and Lock[7] for the oxidation of 1-ethyl-2-pyrrolidinone, because the nmr peaks do not match those given for 2-pyrrolidinone by Mondelli and coworkers.[31] Because it was not deemed important, this very minor product was not identified by other methods. One possible interpretation of the nmr peak placements is that the product was 1-methyl-2-pyrrolidinol.

Table 2-6

Proposed ^{13}C nmr assignments for 1-methyl-2-pyrrolidinol

Carbon	^{13}C(ppm)
1	28.6
2	77.6
3	31.2
4	18.3
5	46.8
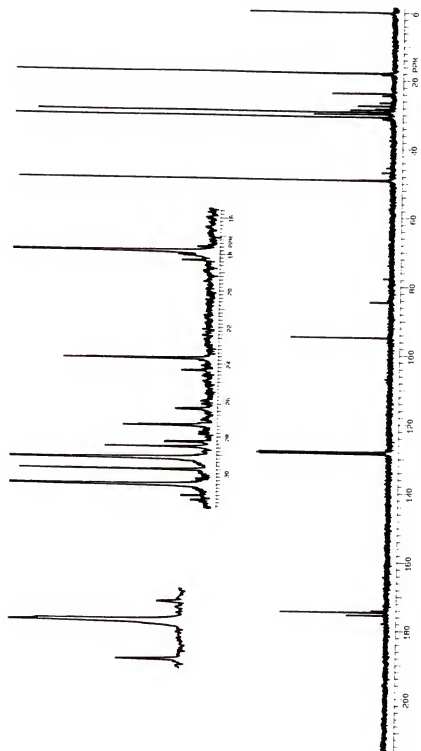
Figure 2-20   13C nmr of 1-methyl-2-pyrrolidinone oxidized for 36
hours at 75oC under 50 psig oxygen(in C6D6, TMS).
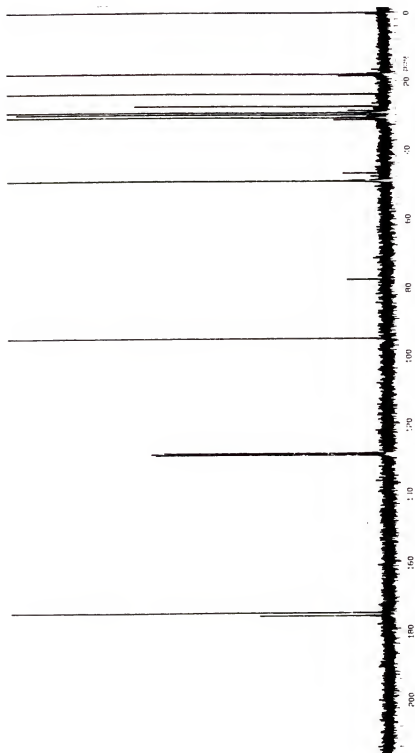
Figure 2-21   13C nmr of 1-methyl-2-pyrrolidinone oxidized for 48 hours at 75°C under 50 psig oxygen(in C_6D_6, TMS).
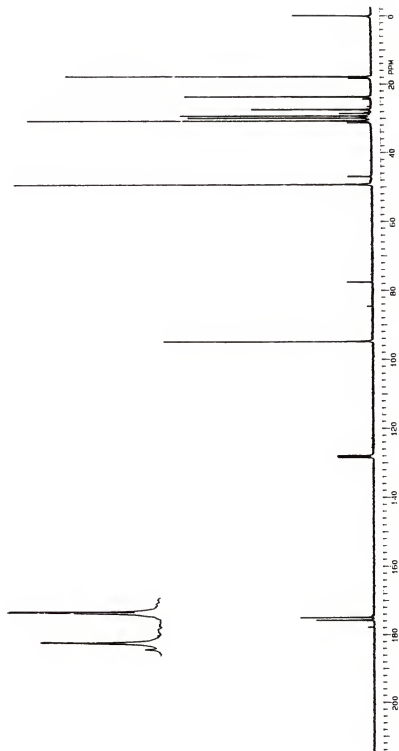
Figure 2-22 ^{13}C nmr of 1-methyl-2-pyrrolidinone oxidized for 48 hours at 75°C under 50 psig oxygen after vacuum distillation at 0.0001mbar and low temperature (in C_6D_6, TMS).

GC-MS data

The major product of the oxidation of 1-methyl-2-pyrrolidinone at 75°C under 50 psig oxygen without a catalyst present is the peroxide, 1-methyl-5 peroxy-2-pyrrolidinone. The nmr data, the GC-MS and IR data support this conclusion. The GC-MS of the oxidized 1-methyl-2-pyrrolidinone was performed on two different instruments because the ITDS GC-MS was not capable of detecting peroxides. The ITDS GC-MS was used to detect the formation of N-methylsuccinimide (figure 2-23) from 1-methyl-2-pyrrolidinone (figure 2-24). The parent ions in figures 2-23 and 2-24 are at 114 and 100 amu (atomic mass unit) respectively, which is one greater than their molecular weights of 99 and 113 amu. This corresponds to the addition of a proton.

The Finnigan single quadrupole mass spectrometer, equipped with a gas chromatograph, containing an on-column injector, was used to observe the peroxide products. Chemical ionization with methane (CH_5^+) was used in response to problems with the stability of the peroxide during ion bombardment.

Interpretation of the peroxide's GC-MS in figure 2-25 is complicated by the use of chemical ionization. In table 2-7 an interpretation of the GC-MS data is given.

The presence of a strong parent ion at 132 amu and the peak at 114 amu, revealing the loss of water from the parent ion, indicated that the peroxide of formula weight 131 had been identified. The parent ion and the decomposition pattern of the mass spectrum (figure 2-25) were evidence of the formation of peroxide by addition of two oxygen atoms to 1-methyl-2-pyrrolidinone.
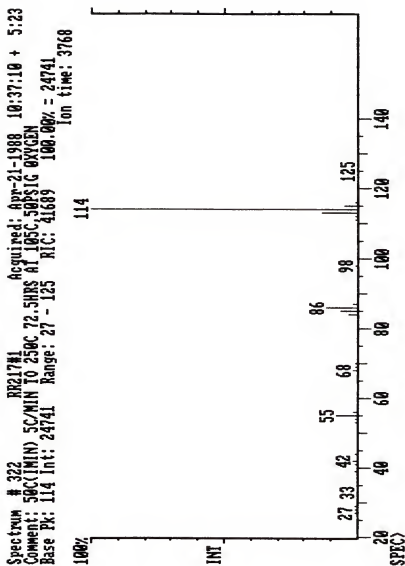
Figure 2-23   GC-MS of N-methylsuccinimide.

Spectrum # 230   Acquired: Apr-17-1988 11:30:56 + 3:51
Comment: 50C(1MIN) 5C/MIN TO 250C
Base Pk: 100 Int: 5411   Range: 27 - 200   RIC: 9800   100.00% = 5411
                                                        Ion time: 13231
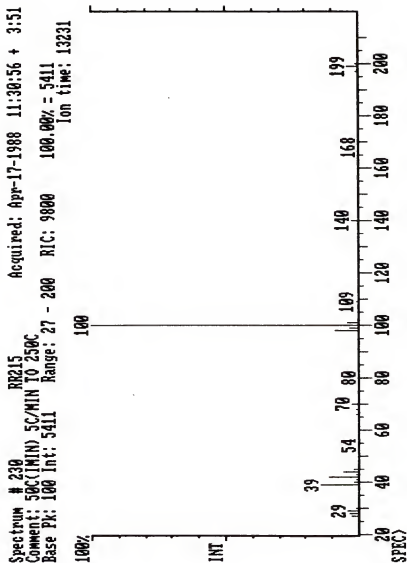
Figure 2-24   GC-MS of 1-methyl-2-pyrrolidinone.
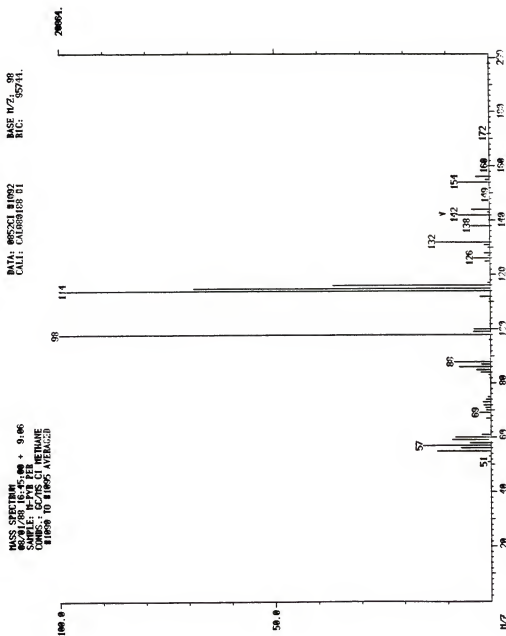
Figure 2-25 GC-MS of 1-methyl-5-peroxy-2-pyrrolidinone by chemical ionization with methane(CH$_5^+$).

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Table 2-7

Interpretation of GC-MS data for 1-methyl-5-peroxy-2-pyrrolidinone[a]

</div>

Species	Parent ion
1-methyl-5-peroxy-2-pyrrolidinone	132[b]
131 + $C_3H_5^+$(41)	172
172 - H_2O(18)	154
131 + $C_2H_5^+$(29)	160
160 - H_2O(18)	142
132 - H_2O(18)	114
131 - OOH(33)	98

(a) formula weight=131   (b) addition of a proton

The loss of water by the parent ion (132 amu) and the ions at 172 and 160 amu resulting in their respective products at 114, 154 and 142 amu, is persuasive evidence that a peroxide was present. The difference between each set of peaks is 18 amu which corresponds to a loss of water from each of the parent ions (132, 172 and 160 amu). During chemical ionization, the presence of peroxide is characterized and confirmed by loss of water. The mass of the parent ion at 132 amu completely ruled out the possibility of an N-oxide similar to N-methylmorpholine N-oxide. The mass spectrum supports our hypothesis that the oxidant was a peroxide. The parent ion at 132 amu also firmly rules out the possibility that the peroxide was a polymeric material.

IR Data

The infrared spectra of the oxidized 1-methyl-2-pyrrolidinone further supports our hypothesis that the oxidant present was indeed the 1-methyl-5

peroxy-2-pyrrolidinone. The IR spectrum of the peroxide in 1-methyl-2-pyrrolidinone (concentrated by vacuum distillation) (figure 2-26) contains a large, relatively sharp O-H stretch for the peroxide at 3200cm^{-1}.[8] The O-H inplane bending is coupled to the C-H wagging, producing two bands at 1330cm^{-1} and 1420cm^{-1}. The band at 1420cm^{-1} is masked by a 1-methyl-2-pyrrolidinone band. There are also C-O stretching bands between 1000 and 1260cm^{-1}, indicating a carbon-oxygen single bond as in an alcohol or peroxide. The broad absorption band between 500 and 850cm^{-1} in figure 2-27 can also be seen in the IR spectra of both methanol and phenol (in liquid or solid phase).[32] All of these distinctions are clarified in figure 2-27 which contains an overlay of the oxidized 1-methyl-2-pyrrolidinone (heavier line) and the pure 1-methyl-2-pyrrolidinone.

The IR data is consistent with the ^{13}C and proton nmr and the GC-MS data in supporting our hypothesis that the oxidation of 1-methyl-2-pyrrolidinone without catalyst (at 75°C under 50 psig oxygen) produces a stable peroxide. The nmr data demonstrates that the peroxide is relatively stable under these conditions, since the peroxide was virtually the sole product of the reaction after 48 hours at 75°C (see figures 2-21 and 2-22).

The peroxide was formed, when 1-methyl-2-pyrrolidinone was oxidized at 105°C under 50 psig oxygen, but it was rapidly decomposed to the N-methylsuccinimide (figure 2-23). The maximum concentration of peroxide in figure 2-28 was attained within six hours and the concentration was lower than the concentration for the oxidation at 75°C (see figure 2-3). At 105°C, rather than form a stable peroxide, the peroxide was rapidly decomposed to the
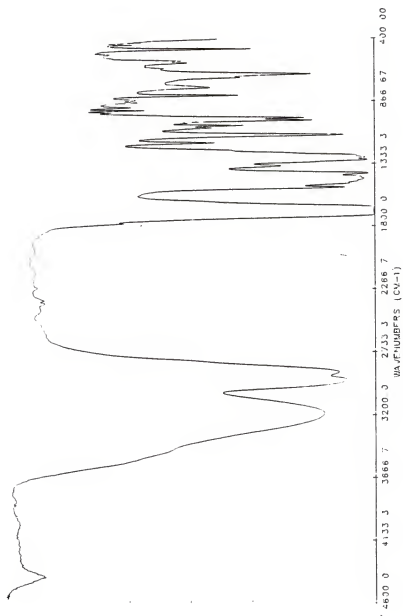
Figure 2-26   IR of oxidized 1-methyl-2-pyrrolidinone in 1-methyl-2-pyrrolidinone.
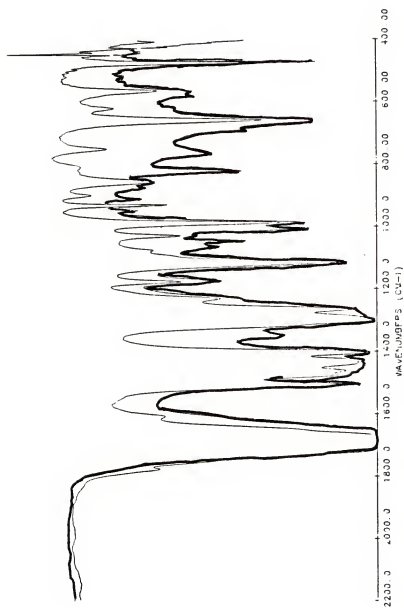
Figure 2-27   IR overlay of oxidized
1-methyl-2-pyrrolidinone and pure
1-methyl-2-pyrrolidinone.
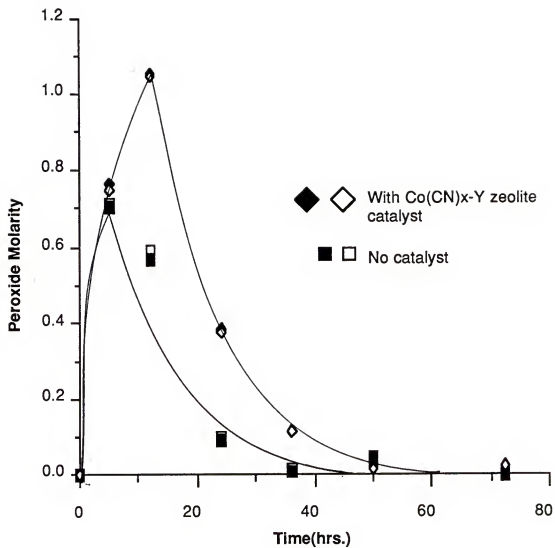
Figure 2-28 Oxidation of 1-methyl-2-pyrrolidinone with and without
Co(CN)x-Y zeolite catalyst at 105 C with 50 psig oxygen.

N-methylsuccinimide by a route similar to the one in equation 17. This was verified by ^{13}C and proton nmr samples taken after 72 hours of oxidation at 105°C. In figures 2-29 and 2-30, the ^{13}C and proton nmr of the solid, filtered from the 1-methyl-2-pyrrolidinone and sublimed, were identical to those for actual samples of N-methylsuccinimide(figures 2-12 and 2-13). The difference in the total amount of oxidation products produced at 75°C and 105°C without catalyst present is displayed in figure 2-31. As seen before in the nmr data, however, after 36 hours, virtually all of the oxidation product produced at 75°C was the 1-methyl-5-peroxy-2-pyrrolidinone, while virtually all of the oxidation product at 105°C was the N-methylsuccinimide. Therefore, in order to produce the stable peroxide of 1-methyl-2-pyrrolidinone for use as an oxidant of organic substrates, the reactions were run at 75°C.

Effect of Catalysts on Peroxide Formation

The behavior of catalysts in the oxidation of 1-methyl-2-pyrrolidinone was predictable and in accord with their behavior as autoxidation catalysts[9], except for that of the Co(CN)$_x$-NaY zeolite catalyst.

CoBPI [BPI = 1,3-bis(2' pyridylimino)isoindolene], Co(octoate)$_2$ (octoate = 2-ethylhexanoate) and TPPMnCl (TPP = tetraphenylporphyrin) all rapidly decomposed the peroxide to the N-methylsuccinimide. In figures 2-7 and 2-32 one can follow the plotted formation of the peroxide over time at 75°C under 50 psig oxygen for the CoBPI and TPPMnCl respectively. In figure2-33, one can see a ^{13}C nmr of a 1-methyl-2-pyrrolidinone oxidation reaction after 24 hours at 75°C with Co(octoate)$_2$ catalyst. Since the titration of the Co(octoate)$_2$ catalyzed solution showed that the oxidized solution did not contain peroxides,
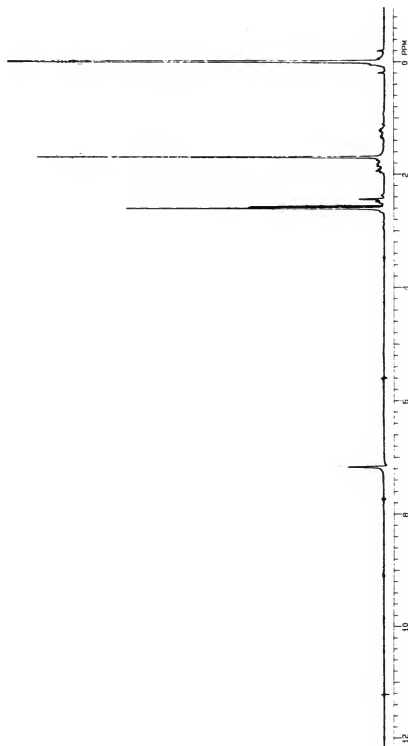
Figure 2-29   Proton nmr of solid(sublimed) from oxidation
of 1-methyl-2-pyrrolidinone at 105°C
(TMS internal standard).
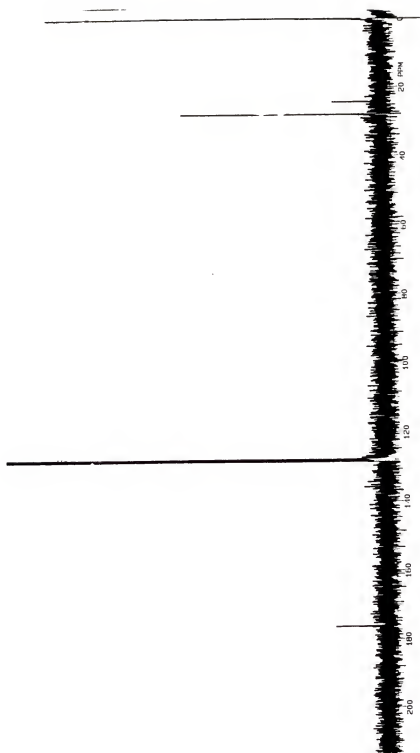
Figure 2-30 13C nmr of solid(sublimed) from oxidation of
1-methyl-2- pyrrolidinone at 105°C
(TMS internal standard).
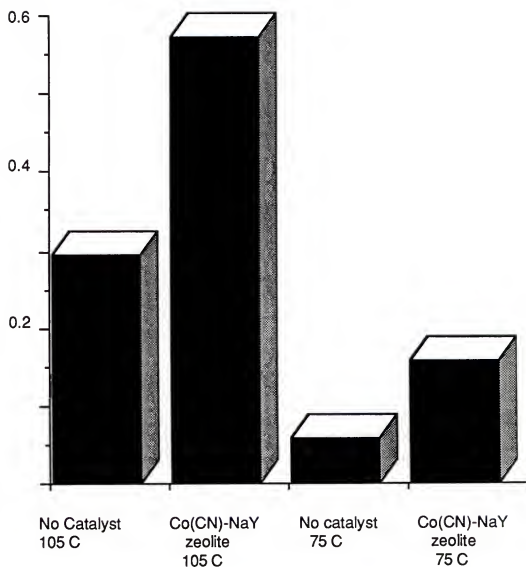
Figure 2-31 Ratio of oxidation products(1-methyl-5-peroxy-2-pyrrolidinone
and N-methylsuccinimide) to 1-methyl-2-pyrrolidinone after
72 hours at 75 C or 105 C under 50 psig oxygen.
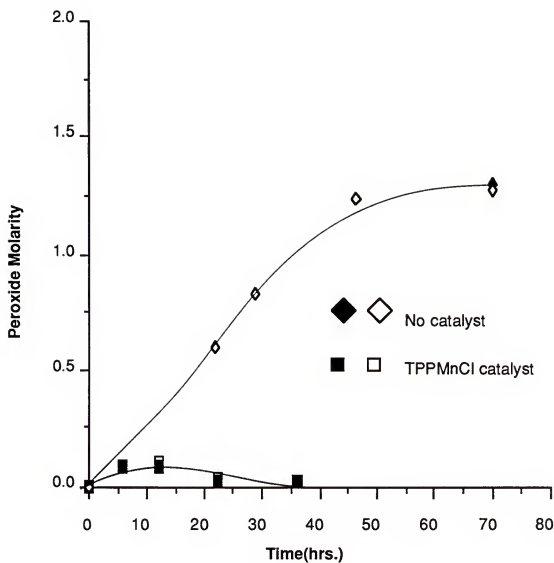
Figure 2-32 Oxidation of 1-methyl-2-pyrrolidinone with and without
TPPMnCl catalyst at 75 C with 50 psig oxygen.

Figure 2-33 ^{13}C nmr of 1-methyl-2-pyrrolidinone oxidized
by Co(octoate)$_2$ at 75°C under 50psig oxygen
for 24 hours (in C_6D_6, TMS).

either Co(octoate)$_2$ was an inhibitor in this reaction or very rapidly decomposed the peroxide to the N-methylsuccinimide. The ^{13}C nmr in figure 2-33 clearly shows that the latter was in fact true. From these three pieces of data one concludes that CoBPI, TPPMnCl and Co(octoate)$_2$ do not inhibit or enhance the formation of peroxide, but do greatly increase its rate of decomposition.

The activity of the Co(CN)$_x$-NaY zeolite catalyst has also been explored by other members of the Drago group.[33] This species has been demonstrated to be capable of selectively adsorbing and desorbing molecular oxygen and in fact enhanced the rate of oxidation of alkenes in 1-methyl-2-pyrrolidinone. It may have taken part in the actual stepwise oxidation of the alkenes, but it is more likely that its effect on these reactions was to augment the quantity of peroxide available for use in these oxidations. Figures 2-34 and 2-35 show that the addition of Co(CN)$_x$-NaY zeolite enhanced the amount of peroxide produced during the reaction at 75°C and 105°C, respectively. It should also be noted that at 75°C there is no induction period prior to the formation of the peroxide of 1-methyl-2-pyrrolidinone when the Co(CN)$_x$-NaY zeolite catalyst is present. In figure 2-31 it is clear that the addition of the Co(CN)$_x$-NaY zeolite catalyst greatly enhanced the total oxidation of 1-methyl-2-pyrrolidinone at both 75°C and 105^{0}C.

The reaction of 1-methyl-2-pyrrolidinone with the Co(CN)$_x$-NaY zeolite catalyst also produces a species that is different from the peroxide and N-methylsuccinimide. In figures 2-35, 2-36 and 2-37, as one follows the reaction's progress, there is a species other than the peroxide being produced
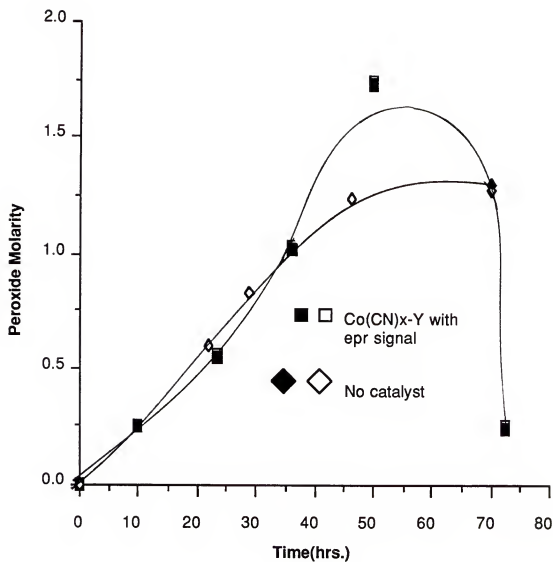
Figure 2-34 Oxidation of 1-methyl-2-pyrrolidinone by Co(CN)x-Y catalyst vs oxidation of 1-methyl-2-pyrrolidinone without catalyst. Both at 75 C with 50 psig oxygen.
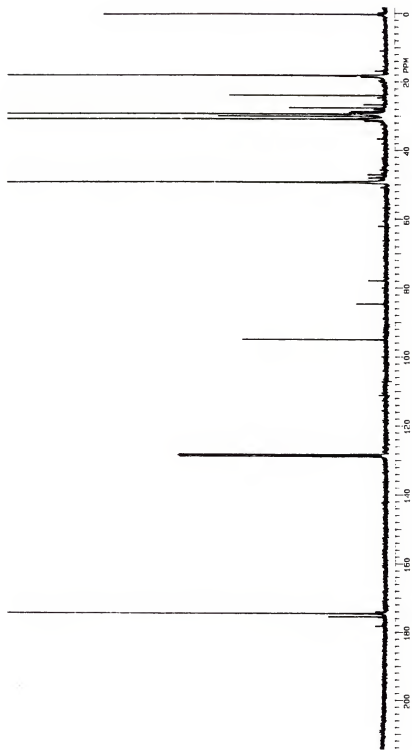
Figure 2-35   13C nmr of 1-methyl-2-pyrrolidinone oxidized
10 hours by Co(CN)$_x$-NaY zeolite at 75°C,
50 psig oxygen (in C$_6$D$_6$; TMS).
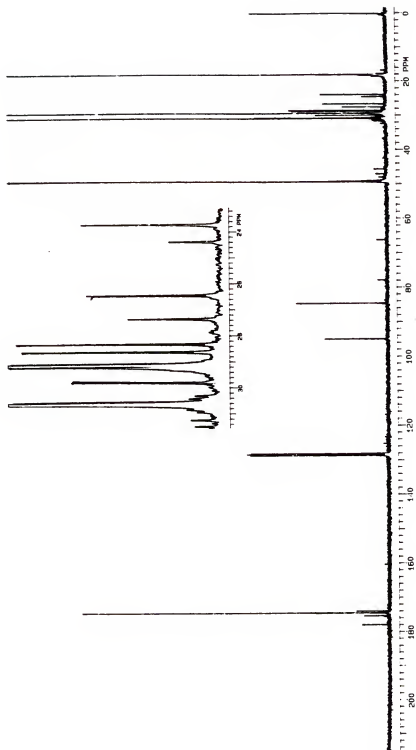
Figure 2-36 ^{13}C nmr of 1-methyl-2-pyrrolidinone oxidized 24 hours by $Co(CN)_x$-NaY zeolite at 75°C, 50 psig oxygen (in C_6D_6, TMS).
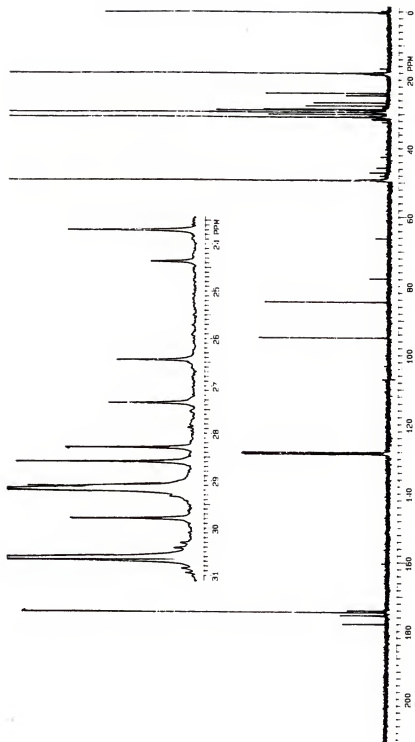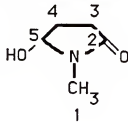
Figure 2-37 ^{13}C nmr of 1-methyl-2-pyrrolidinone oxidized 24 hours by Co(CN)$_x$-NaY zeolite at 75°C, 50 psig oxygen (in C$_6$D$_6$; TMS).

in the oxidation reaction when the Co(CN)$_x$-NaY zeolite is present. New peaks at 26.3, 28.6, 29.1, 84.4 and 173.8ppm are observed. All other large peaks present are accounted for by the 1-methyl-2-pyrrolidinone, N-methylsuccinimide and the 1-methyl-5-peroxy-2-pyrrolidinone. This new species is most likely the 5-alcohol of 1-methyl-2-pyrrolidinone shown in table 2-8.

The assignments were made using the DEPT program on the XL-300. Comparing the ^{13}C nmr shift from 49.4ppm to the peak at 84.4ppm to that of the ^{13}C nmr shift from the C-H of cumene to the C-OH of cumyl alcohol (table 2-5), it becomes quite clear that the added oxygen is similar to that of an alcohol.

<u>Table 2-8</u>
^{13}C nmr peak assignments for 1-methyl-5-hydroxy-2-pyrrolidinone

	Carbon	^{13}C(ppm)
	1	26.3
	2	173.8
	3	29.1
	4	28.6
	5	84.4

The data in table 2-5 shows a carbon 1 ^{13}C nmr shift of 38ppm for cumene to cumyl alcohol. The ^{13}C nmr shift from 1-methyl-2-pyrrolidinone to the 5-alcohol was 35ppm, which is close to the shift for cumyl alcohol and further supports the interpretation of the data given by the DEPT program, which showed that, like the carbon 5 of the peroxide, that of the alcohol had only one proton attached to it, suggesting that the oxygenated species contains a single bond between the carbon 5 of the pyrrolidinone ring and the added oxygen atom. The alcohol is

most likely further oxidized to the N-methylsuccinimide during the course of the reaction.[15,34]

This interpretation of the ^{13}C nmr data is supported by Silverstein and Bassler,[32] who reported that replacing -H by -OH causes a downfield shift of 35-52ppm for alcohols. As indicated in table 2-8, a shift of 35ppm was in fact observed for the alcohol product. A 5-12ppm downfield shift was also expected for carbon 4 and an upfield shift of 0-6ppm was expected for carbon 3. A downfield shift of 10.4ppm was observed for carbon 4 and an upfield shift of 1.7ppm was observed for carbon 3. The 5-alcohol of 1-methyl-2-pyrrolidinone therefore satisfies the requirements for an alcohol and explains the five new peaks observed in the ^{13}C nmr of 1-methyl-2-pyrrolidinone oxidized in the presence of Co(CN)$_x$-NaY zeolite. Other than the fact that it produces a new species, the 5-alcohol of 1-methyl-2-pyrrolidinone, the Co(CN)$_x$-NaY zeolite oxidation of 1-methyl-2-pyrrolidinone is of interest because it produces more of the peroxide than do those reactions without catalyst. The work of Sagar and his coworkers[8,9] indicates that the introduction of transition-metal catalysts does not greatly enhance or inhibit the oxidation of alkylamides to their peroxides in low concentrations (2ppm), but does enhance the formation of the stable imides from the peroxides and, at high concentrations (50ppm), greatly enhances the rate of formation of the stable products (imides) at 131°C. Accordingly, our catalysts CoBPI, Co(octoate)$_2$ and TPPMnCl decomposed the peroxide to the N-methylsuccinimide even when their concentrations were between 0.5ppm and 2ppm, whereas the Co(CN)$_x$-NaY zeolite enhanced the formation of the peroxide.

To determine why the Co(CN)$_x$-NaY zeolite enhanced the formation of the 1-methyl-5-peroxy-2-pyrrolidinone (figures 2-32 and 2-34), a series of experiments with the components of the Co(CN)$_x$-NaY zeolite were performed. When a Co(CN)$_x$NaY zeolite catalyst with a large epr signal, indicating the presence of a cobalt-dioxygen adduct, was compared to a catalyst with little or no oxygen adduct present, the catalyst with the large epr signal was definitely the better of the two catalysts (figure 2-38). From this experiment, it seemed that the cobalt-dioxygen adduct had an important role in the oxidation of 1-methyl-2 pyrrolidinone to the peroxide. There was, however, a simpler explanation based on the amount of free cobalt(II) in the NaY zeolite cages. These "free" cobalt(II) (without cyanide ligands) in the large supercages and smaller sodalite cages of the Y zeolite were potentially responsible for the increased oxidation of 1-methyl-2-pyrrolidinone in the presence of the Co(CN)$_x$-NaY zeolite catalyst. Figure 2-39 demonstrates that this was indeed the case, a Co-NaY zeolite catalyst containing 4 Co(II)/fwu (fwu=formula weight unit) oxidized 1-methyl-2-pyrrolidinone at a faster rate and to a greater extent than did a Co(CN)$_x$-NaY zeolite with the same number of cobalt/fwu. The Co-NaY zeolite greatly increased the quantity of peroxide produced and, like the Co(CN)$_x$-NaY zeolite catalyst, eliminated the 20 hour induction period which was present for the uncatalyzed oxidation of 1-methyl-2-pyrrolidinone (figure 2-40). The oxidative ability of the Co(CN)$_x$-NaY zeolite apparently depended on the pretreatment of the catalyst at elevated temperatures up to and including 300°C. The oxidation product yield increased as the pretreatment temperature rose. This could be explained by the dehydration of the free Co(II) in the Y
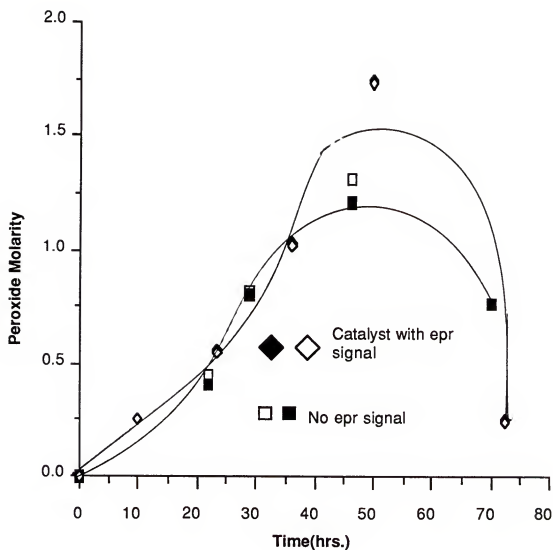
Figure 2-38 Oxidation of 1-methyl-2-pyrrolidinone by Co(CN)x-Y with and without cobalt-dioxygen adduct epr signal at 75 C with 50 psig oxygen.
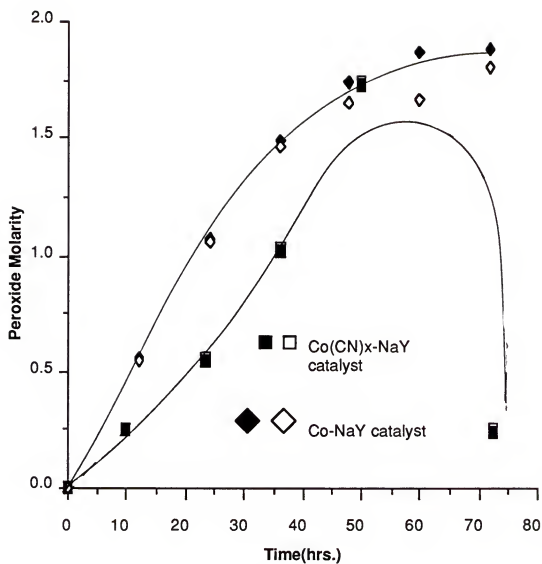
Figure 2-39 Oxidation of 1-methyl-2-pyrrolidinone by
Co(CN)x-NaY and Co-NaY catalysts
(both dried at 150 C) at 75 C under
50 psig oxygen.
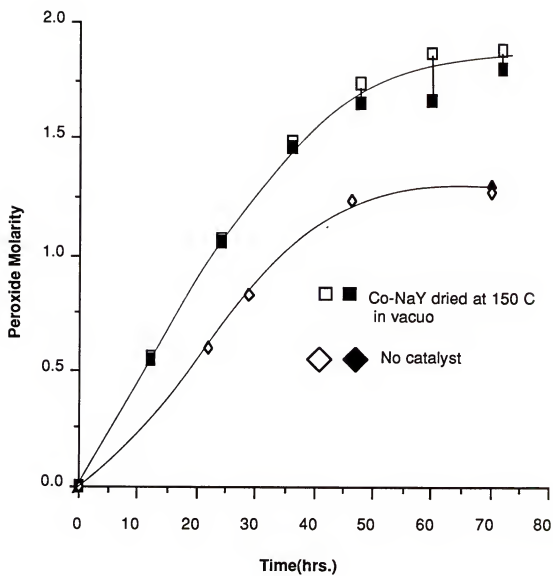
Figure 2-40 Oxidation of 1-methyl-2-pyrrolidinone with and
without Co-NaY catalyst at 75 C and 50 psig oxygen.

zeolite. This is, however, diminished somewhat by their movement from the large supercages to the smaller, less accessible sodalite cages. In figure 2-41, the initial rates for the catalyst, dried at room temperature and 150°C, are the same for the first 48 hours, but after 48 hours there was a drop in the product yield for the catalyst dried at room temperature. The Co-NaY zeolite (pretreated at 150°C) started to gradually level off at the same point in time, but did not drop. For the first 36 hours, the yields were the same. It may not matter greatly, therefore, where the free cobalt (II) is in the zeolite structure, unless 150°C is not a high enough temperature to drive the Co (II) into the sodalite cages.

That it is indeed the free Co (II), and not the NaY zeolite, that is the active species, can be seen in figure 2-42. NaY zeolite appears to inhibit the formation of the peroxide (figure 2-43). The free Co (II) in the NaY zeolite must, therefore, be the active species in the oxidation of 1-methyl-2-pyrrolidinone to 1-methyl-5-peroxy-2-pyrrolidinone by the $Co(CN)_x$-NaY zeolite since the presence of the cyano cobalt (II) anion and the NaY zeolite do not increase the oxidation yield of 1-methyl-2-pyrrolidinone. The cyano cobalt (II) anion is not necessary for the augmentation of oxidation products and the NaY zeolite by itself inhibits the oxidation of 1-methyl-2-pyrrolidinone to the peroxide. Since the $Co(octoate)_2$ does not enhance the yield of peroxides, but the Co-NaY zeolite does, it appears that it is the restrictions provided by the Y zeolite structure which allow the 1-methyl-2-pyrrolidinone into the structure to be oxidized by the Co(II). It does not, however, increase the rate of decomposition like the other cobalt catalysts, such as CoBPI and $Co(octoate)_2$.
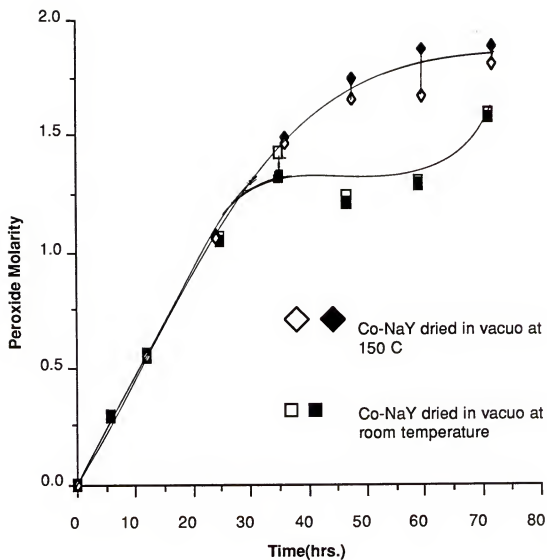
Figure 2-41 Oxidation of 1-methyl-2-pyrrolidinone by Co-NaY dried
at room temperature and 150 C in vacuo. Oxidations
were performed at 75 C with 50 psig oxygen.

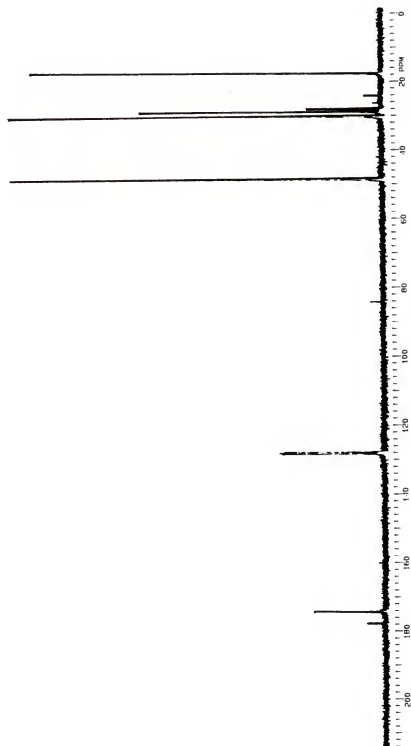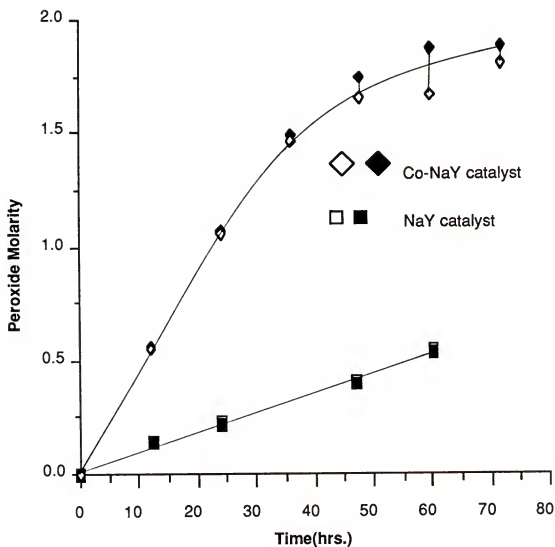Figure 2-42 Oxidation of 1-methyl-2-pyrrolidinone at 75 C under 50 psig oxygen. Co-NaY and NaY were dried prior to use at 150 C in vacuo.
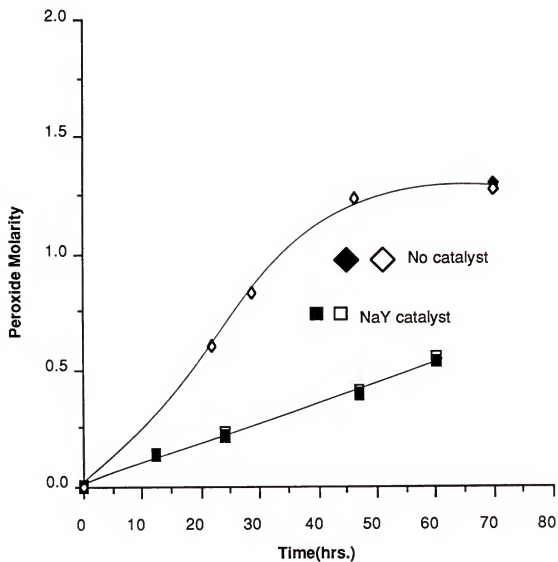
Figure 2-43 Oxidation of 1-methyl-2-pyrrolidinone with and without NaY catalyst at 75 C under 50 psig oxygen.

We found a good source of oxidant in the 1-methyl-5-peroxy-2pyrrolidinone, good in that it was relatively simple to generate and both a good oxidant of triphenyl phosphine to its oxide and stable at high temperatures (75°C). We attempted to make the peroxide a more specific oxidant by changing the reactivity of the pyrrolidine ring by attaching a methyl group at that site. This was also done in an attempt to halt the formation of the final oxidation product, N-methylsuccinimide, by generating an alcohol instead. This alcohol could be reoxidized by molecular oxygen to the peroxide. This was done because attempts to reoxidize the N-methylsuccinimide to 1-methyl-2-pyrrolidinone with Pt (IV) oxide in ethanol at 75°C under 55°C psi hydrogen were only marginally successful. Small amounts of 1-methyl-2-pyrrolidinone were detected after 264 hours of reaction. In the literature, there is an electrochemical technique for the reduction of N-methylsuccinimide to the 1-methyl-2-pyrrolidinone.[35]

The 1,5-dimethyl-2-pyrrolidinone was successfully oxidized to its peroxide (figure 2-44) and was utilized successfully for the oxidation of alkene substrates. Comparison with 1-methyl-2-pyrrolidinone (figure 2-45) showed that it could be oxidized to the peroxide in slightly higher yields than 1-methyl-2-pyrrolidinone. The change in the ^{13}C nmr of the pure 1,5-dimethyl-2-pyrrolidinone in figure 2-46 to that in figure 2-47 after 24 hours of oxidation at 75°C indicates that a product was being formed and was accumulating as the reaction proceeded. The titration data in figure 2-44 and the ^{13}C nmr peak placement in figure 2-47 suggest that that product is the peroxide of 1,5-dimethyl-2-pyrrolidinone. The appearance of new peaks at 97.4 and 175.0ppm indicates that a stable
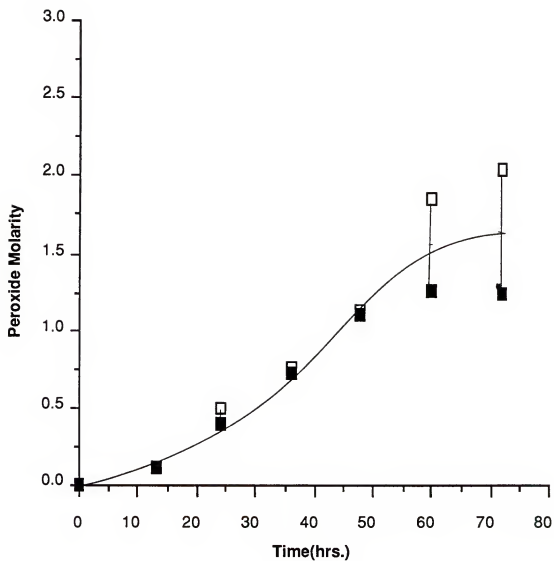
Figure 2-44 Oxidation of 1,5-dimethyl-2-pyrrolidinone without catalyst
at 75 C and 50 psig oxygen.
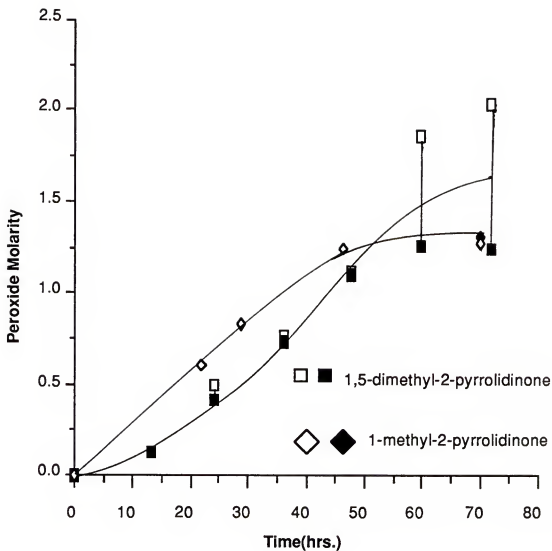
Figure 2-45 Oxidation of 1,5-dimethyl-2-pyrrolidinone and 1-methyl-2 pyrrolidinone without catalyst at 75 C with 50 psig oxygen.
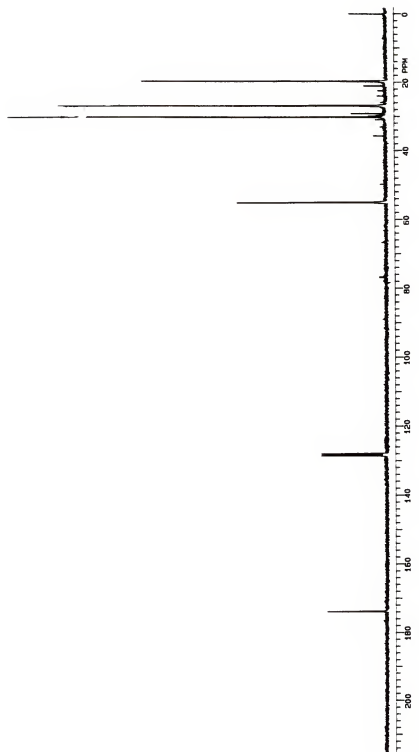
Figure 2-46 ^{13}C nmr of 1,5-dimethyl-2-pyrrolidinone (in C_6D_6, TMS).
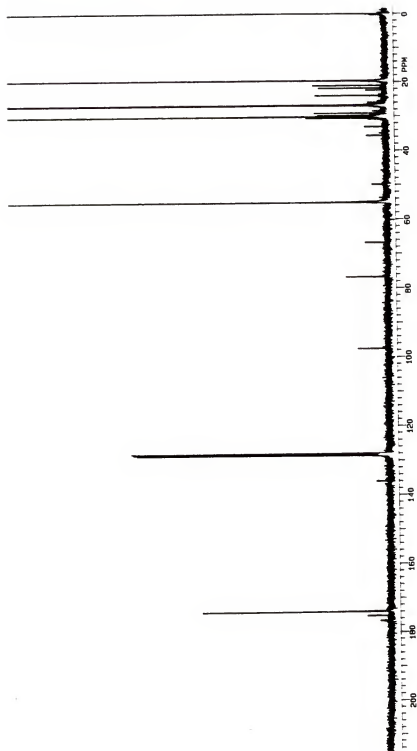
Figure 2-47   13C nmr of 1,5-dimethyl-2-pyrrolidinone oxidized 24 hours at 75°C under 50 psig oxygen (in C_6D_6, TMS).

peroxide is being formed during the reaction. These two peaks parallel those for carbon 5 and carbon 2 of the 1-methyl-5-peroxy-2-pyrrolidinone in table 2-4.

The proton nmr of the pure 1,5-dimethyl-2-pyrrolidinone in figure 2-46 and that of a sample taken after 12 hours of oxidation at 75°C in figure 2-47 indicate that some changes in the 1,5-dimethyl-2-pyrrolidinone were occurring during the reaction because the peaks at 1.0, 1.9 and 3.3ppm were smaller in figure 2-49 than in figure 2-48. Proton/carbon 2-d correlation nmr and DEPT were not run on this sample to determine what peaks were shifting. An unfortunate problem with this solvent was that the final oxidation product, the 5-alcohol, could not be reoxidized to the peroxide for further use as an oxidant. The 1,5-dimethyl-2-pyrrolidinone was no more active in the oxidation of alkenes than was the 1-methyl-2-pyrrolidinone.

Although a racemic mixture of the 1,5-dimethyl-2-pyrrolidinone was used for these reactions, it should be possible to use optically active N-methylpyrrolidinones, substituted at the 5-position, for asymmetric epoxidations. The oxidation of the 1,5-dimethyl-5-peroxy-2-pyrrolidinone to the 1,5-dimethyl-5-peroxy-2-pyrrolidinone proves that a tertiary carbon, adjacent to the nitrogen of a pyrrolidinone ring, can be oxidized to the peroxide. This may lead to a new series of chiral peroxides which are capable of asymmetric epoxidations similar to those of Sharpless and his coworkers.[36] The metal catalyzed epoxidations are believed to proceed by a metal-alkyl hydroperoxide complex mechanism in which the oxidant is the metal-alkyl hydroperoxide(A) rather than the metal-peroxide(B).[30,37]
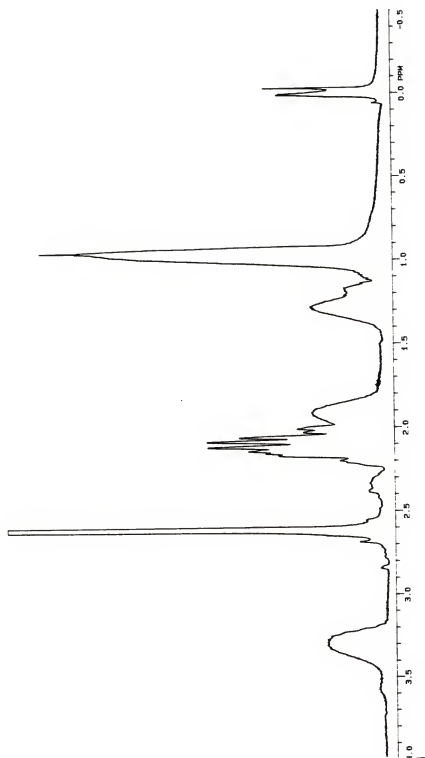
Figure 2-48   Proton nmr of 1,5-dimethyl-2-pyrrolidinone (in C_6D_6, TMS).
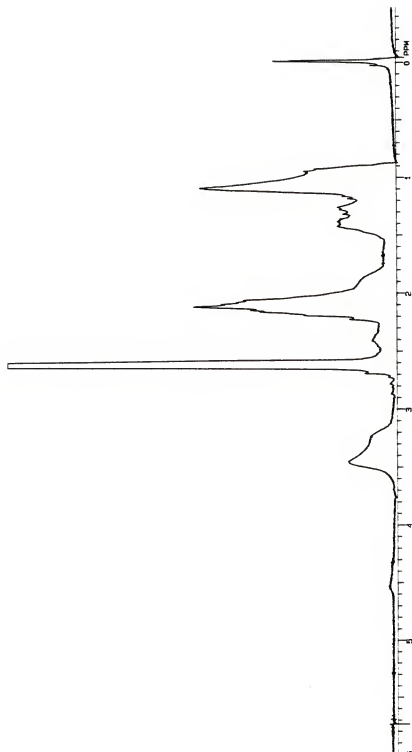
Figure 2-49   Proton nmr of 1,5-dimethyl-2-pyrrolidinone oxidized 12 hours at 75°C, 50 psig oxygen (in C_6D_6, TMS).
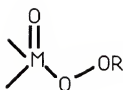
(A)   (B)

A chiral peroxide should, therefore, increase the stereospecificity of the reaction, allowing the asymmetric epoxidation of alkenes.

<u>Oxidation of L-Prolinamide</u>

Another approach to these oxidation reactions was to look at the structure of cytochrome P-450 and look for pyrrolidinones and pyrrolidine rings attached to carbonyl groups which were incorporated into the external structure of the molecule. Due to the ease of oxidation of the pyrrolidinone ring to the peroxide, it may be that this is the active species in the oxidation of organic substrates by the cytochrome P-450. The amino acid, proline, is incorporated into the external structure of the cytochrome P-450 in the manner shown below.
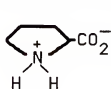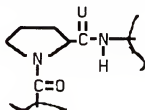
proline   proline bonding in cytochrome P-450

In the cytochrome P-450, the nitrogen atom of the proline is adjacent to a carbonyl functionality which makes it an amide. The two carbon atoms at positions 1 and 5 on the proline ring are similar to carbon 5 of a 2-pyrrolidinone and may be easily oxidized to the peroxide like 1-methyl-2-pyrrolidinone. The

proline's pyrrolidine ring should be oxidized at relatively low temperatures to its peroxide in the same way that the 1-methyl-2-pyrrolidinone was oxidized.

An acylated prolinamide was used to model proline in cytochrome P-450 in order to determine whether or not it was capable of forming a peroxide similar to those formed by the pyrrolidinones. L-prolinamide was acylated by an adapted literature method.[29] The final product was separated from triethylammonium hydrochloride by filtration and gave the ^{13}C nmr in figure 2-50.

The ^{13}C nmr in figure 2-51 is that of the starting material: L-prolinamide. The peak assignments for the ^{13}C nmr of the L-prolinamide in figure 2-49 are in table 2-9 and are based on the assignments for the 1-methyl-2-pyrrolidinone. The peak assignments for the acylated L-prolinamide of figure 2-50 are in table 2-10. Titration of 1ml samples after 18 hours of oxidation at room temperature in acetonitrile under 50 psig oxygen showed that there was a small amount of peroxide in the acylated L-prolinamide and none in the L-prolinamide. The samples were then place in oil baths at 50°C under 50 psig oxygen for 27 hours. After 27 hours, 1ml samples of the two prolinamides were titrated and again only the acylated prolinamide indicated the presence of peroxide.

Table 2-9
^{13}C nmr peak assignments for L-prolinamide
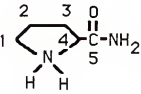
Carbon	^{13}C(ppm)
1	47
2	26
3	31
4	61
5	179

Figure 2-50 ^{13}C nmr of acylated L-prolinamide contaminated by Et$_3$NHCl and CH$_2$Cl$_2$ (in CDCl$_3$, TMS).
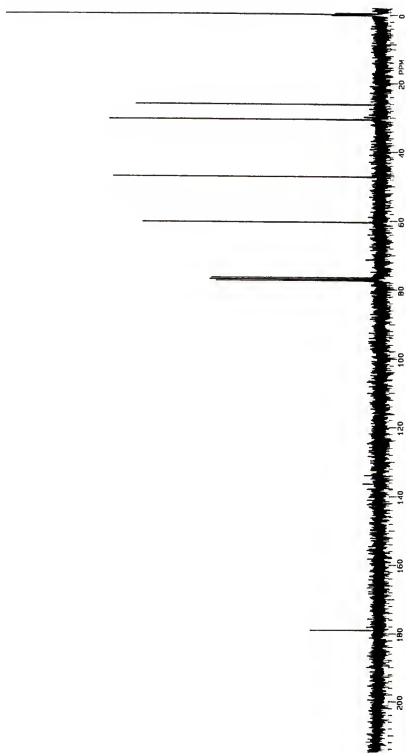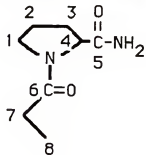
Figure 2-51 ^{13}C nmr of L-prolinamide(in CDCl$_3$, TMS).

Table 2-10
^{13}C nmr peak assignments for acylated prolinamide

Carbon	^{13}C(ppm)
1	48.6
2	24.9
3	29.0
4	59.9
5	175.1
6	171
7	32
8	22.4

The acylated L-prolinamide was 0.082M in peroxide indicating that one-third of the acylated prolinamide was converted to the peroxide.

Two other tests for the peroxide were performed in which it was noted that the peroxide concentration was high only in the acylated prolinamide. When the oxidized acylated L-prolinamide was added to an aqueous solution of potassium iodide, the solution quickly turned yellow. The color change was accompanied by vigorous bubbling. Under identical conditions, hydrogen peroxide reacted in the same way. In the second test, the oxidized prolinamide and oxidized acylated prolinamide solutions were added to sodium iodide which had been dissolved in isopropanol with acetic acid. Upon addition of the oxidized acylated L-prolinamide to the NaI solution, it turned very dark, almost black, and it appeared that solid iodine formed. When the dark solution was briefly shaken, the color immediately disappeared.

Throughout all of the tests, the oxidized L-prolinamide solution did not react positively once. It is, therefore, only the amide of the pyrrolidine ring which will easily oxidize to the peroxide at low temperatures. The pyrrolidine ring of

L-prolinamide was more difficult to oxidize without the carbonyl group adjacent to the ring nitrogen and, under the conditions discussed above, was not oxidized at all. This model showed that it is possible to activate the pyrrolidine ring of the amino acid by adding a carbonyl group adjacent to the ring nitrogen. The acylation of the pyrrolidine, therefore, greatly facilitates the formation of a peroxide at a ring carbon adjacent to the nitrogen. This supports our theory that the oxidation of an external proline in cytochrome P-450 may be an alternative pathway for oxidation by cytochrome P-450.

<div align="center">Conclusion</div>

As expected the assignment of the ^{13}C and proton nmr peaks for 1-methyl 2-pyrrolidinone and N-methylsuccinimide facilitated the identification of the product peaks through comparison to those of the N-methylsuccinimide and 1-methyl-2-pyrrolidinone and the oxides of cumene. The identification of the 1-methyl-5-peroxy-2-pyrrolidinone was confirmed by the GC-MS and IR data and, although predicted by the literature, the peroxide was unique in several ways. It was a strong oxidant, yet was stable at temperatures up to 75°C. It was also easily generated with molecular oxygen at temperatures as low as 50°C (The lower limit was found for the air oxidation of the acylated prolinamide with 50 psig oxygen.). The oxidation of 1,5-dimethyl-2-pyrrolidinone to its peroxide is intriguing because it suggests that chiral alkyl hydroperoxides can be

generated from chiral pyrrolidinones. This would be possible if the starting pyrrolidinone were to have a chiral singly substituted carbon 5 which could be oxidized to form a chiral alkyl hydroperoxide.

The generation of the 1-methyl-5-peroxy-2-pyrrolidinone at low temperatures and the electrochemical reduction of the N-methylsuccinimide[40] to the 1-methyl-2-pyrrolidinone suggest that 1-methyl-2-pyrrolidinone can easily generate an alkyl hydroperoxide which could be recycled following its decomposition to N-methylsuccinimide. The recyclable nature of the oxidant, combined with the fact that the 5-substituted pyrrolidinone (1,5-dimethyl-2 pyrrolidinone) was also easily oxidized to its peroxide by molecular oxygen at 75°C, demonstrates that the 1-methyl-2-pyrrolidinones are potentially an excellent source of oxidants for the asymmetric epoxidation of alkenes. The metal-alkyl hydroperoxide formed by a chiral hydroperoxide with a metal complex may be a good catalyst for the asymmetric epoxidation of alkenes similar to those of Sharpless[28,36] and Yamada.[39] The oxidation of alkenes by a chiral alkyl hydroperoxide and a non-chiral metal complex may duplicate the results of Sharpless[28] without the problems caused by unstable chiral metal complexes. The peroxides of 1-methyl-2-pyrrolidinones have been demonstrated to be stable at elevated temperatures(75°C) and are potential oxidants for use in combination with the more stable, non-chiral transition metal complexes.

Another point of interest is the unusual behavior of the $Co(CN)_x$-NaY zeolite catalyst. In his work with the peroxides of the alkylamides, Sagar[8] notes that transition-metal complexes do not enhance the yield of peroxides, but rather,

increase the decomposition rate of the peroxides. The "free" Co(II) in the NaY zeolite enhances the yield of peroxide and in the case of the Co-NaY zeolite does not appear to decompose the peroxide. $Co(CN)_x$-NaY zeolite begins to decompose the peroxide after 48 hours, but this may be due to the $Co(CN)_6^{3-}$ trapped in the larger supercages of the zeolite. In figure 2-31, it is obvious that the addition of the $Co(CN)_x$-NaY zeolite greatly increases the yield of oxidation products of 1-methyl-2-pyrrolidinone over that of the non-catalyzed oxidations. Co-NaY is therefore a useful cocatalyst for the oxidation of organic substrates by metal-alkyl hydroperoxides in 1-methyl-2-pyrrolidinone as it increases the amount of peroxides available for oxidation.

Although the oxidation of the prolinamides was performed in acetonitrile, there is no indication that the peroxides formed were the peroxymidic acid,[40,41] since the solution containing L-prolinamide did not generate peroxides after 18 hours of stirring at room temperature or after 27 hours of stirring at 50°C. Under these conditions, the acylated prolinamide must, therefore, be the sole source of peroxides.

The oxidation of an acylated prolinamide at low temperatures (room temperature and 50°C) may provide an alternate explanation for the cytochrome P-450 oxidation mechanism in natural systems. The ease with which the acylated prolinamides oxidized to the peroxide supports the supposition implicit in the acylation. A pyrrolidine-ring carbon, adjacent to the ring nitrogen, can be more easily oxidized by the addition of a carbonyl group, bonded to the ring nitrogen either as a part of the ring, as in the pyrrolidinones, or simply attached to the nitrogen as a ligand. The amides formed in this way

are easily oxidized at relatively low temperatures and pressures. This strongly suggests that the amino acids containing a pyrrolidine ring such as proline are oxidizable at low temperatures to their peroxides when incorporated into cytochrome P-450.

OXIDATION OF ALKENES, ALKANES AND ALKYL SULFIDES

Background

The oxidation of alkenes to their epoxides is an essential industrial reaction today because the epoxide functional group is a crucial building block in organic synthesis. Epoxides are used in the synthesis of glycols, polymers, polyesters and polyurethanes.[42] The synthesis of epoxides with a carbon chain length of three or more has always been difficult and low in yield for vapor-phase epoxidation. The usual route for vapor-phase oxidation of propene has been to pass propene and oxygen over a fixed bed of bismuth molybdate catalyst at temperatures between 425 and 500°C.[43,44] However,this reaction produces acrolein and, in the presence of ammonia, acrylonitrile.[45,46]

The industrial method for making the epoxide of propylene is currently based on organic hydroperoxides. The Halcon or Oxirane process[47] uses alkyl hydroperoxides for the oxidation of propylene in solution.[48,49] The alkyl hydroperoxides commonly used in this reaction are prepared by the autoxidation of isobutane or ethylbenzene. The economic feasibility of the Halcon process is contingent upon the going price of the co-product alcohols.[50] The yields and the selectivity are, fortunately, very high for the alkyl

hyroperoxide route and make this process financially advantageous.[50]

In the Halcon process, the selectivity for the epoxide product was greatly enhanced by the choice of catalyst. Rhenium catalysts converted 100% of the peroxide present with only a 10% efficiency for the production of the epoxide. Molybdenum and tungsten catalyst converted 80 to 90% of the peroxide with 65 to 71% efficiency for the production of propylene oxide. Vanadium complexes have also been used for these oxidations. Molybdenum, vanadium and tungsten compounds generally give consistently high epoxide yields. The tungsten compounds are the best catalysts when the oxidant is hydrogen peroxide, while the molybdenum and vanadium catalysts are the most effective when alkyl hydroperoxides are used as the oxidant.[48]

The metal-catalyzed oxidations can be divided into two types: heterolytic and homolytic. Homolytic oxidations have free-radical intermediates and are catalyzed by first-row transition metals with one-electron reductions (e.g., Co^{III}/Co^{II}). The hydrocarbon substrate is oxidized outside the metal's coordination sphere and the oxidation is not selective.[51,52] The more selective heterolytic oxidations generally require activation of the substrate by coordination to the metal. They do not have free-radical intermediates and are therefore far more selective and stereospecific than the homolytic oxidations. The heterolytic metal-catalyzed oxiations use second and third-row transition metals which either undergo 2-electron reductions or conserve their oxidation state (e.g., $Mo(CO)_6$).

The homolytic metal-catalyzed oxidation of alkenes involves an outer-sphere electron-transfer mechanism. A good example of this mechanism is the

oxidation of toluene to benzyl acetate by $Co^{III}W_{12}O_{40}^{5-}$. The mechanism for this reaction involves an outer-sphere, electron-transfer mechanism in which the first step in the reaction is the formation of a tolyl radical cation, followed in the second step by the loss of a proton to yield a benzylic radical. The benzylic radical transfers an electron to a second $Co^{III}W_{12}O_{40}^{5-}$. Solvolysis of the benzylic radical gives the final product, benzylic acetate.[53-55]

$$ArCH_3 + Co^{III}W \rightarrow ArCH_3^{\bullet+} + Co^{II}W \qquad (1)$$

$$ArCH_3^{\bullet+} + B: \rightarrow ArCH_2^{\bullet} + BH^+ \qquad (2)$$

$$ArCH_2^{\bullet} + Co^{III}W \rightarrow ArCH_2^+ + Co^{II}W \qquad (3)$$

$$ArCH_2^+ + HOAc \rightarrow ArCH_2OAc + H^+ \qquad (4)$$
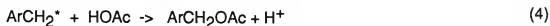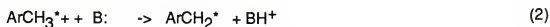
This reaction was also studied using p-methoxytoluene, which gave results similar to those for toluene.[53,54] The acetoxylation of toluene also occurs during this reaction, when it is run under non-aqueous conditions.[53] Similar results were obtained with the $MMo_9O_{32}^{6-}$ (M= Ni^{IV} or Mn^{IV}) heteropolyanions.[56] The 9-heteropolymolybdates were, however, two electron acceptors, and the reaction solutions contained M^{2+} after reaction, indicating that the heteropolyanions had decomposed during the reaction. The yield of benzylacetate was approximately 14.5 mole percent based on the $Co^{III}W_{12}O_{40}^{5-}$ and 44 mole percent based on $Mn^{IV}Mo_9O_{32}^{6-}$ heteropolyanions.[53-56] The product yield is improved, therefore, even though the 9-molybdomanganate(IV) species decomposes during the reaction.

The metal-catalyzed homolytic decomposition of alkyl hydroperoxides generates alkoxy and alkyl peroxy radicals which initiate free-radical chain reactions. They are generated by the following one-electron redox processes:

$$M^{n+} + ROOH \longrightarrow M^{(n-1)+} + RO_2 \cdot + H^+ \tag{6}$$

$$M^{(n-1)+} + ROOH \longrightarrow M^{n+} + RO \cdot + OH^- \tag{7}$$
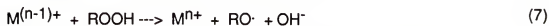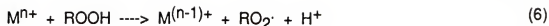
The overall reaction for this process is shown below in equation 8.

$$2ROOH \longrightarrow ROO \cdot + RO \cdot + H_2O \tag{8}$$

$$(9)$$
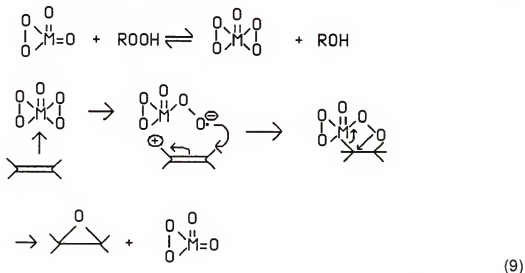
The two mechanisms currently accepted for the metal-catalyzed epoxidation of alkenes have been proposed by Mimoun [50,55] and Sharpless.[56-59] The Mimoun mechanism (equation 9) involves a metal-peroxide intermediate formed by reaction of the oxometal (M=O) group with an alkyl hydroperoxide. The alkyl portion of the peroxide is lost as an alcohol and does not effect the stereochemistry of the reaction.

In an [18]O labelling experiment, Sharpless and coworkers[62] demonstrated, however, that the epoxide oxygen arises exclusively from the peroxide. The Mimoun mechanism shown above in equation 9 does not distinguish between metal-peroxide oxygen atoms on the catalyst prior to the addition of peroxide and those added to the metal-peroxide complex by the alkyl hydroperoxide. Sharpless proposed the following intermediate for the metal

catalyzed epoxidation of olefins which uses a metal-alkyl hydroperoxide complex mechanism:[62]
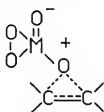
(10)

He later proposed a mechanism for the reaction which involved this intermediate[42,59,60] (in equation 10) in the epoxidation of alkenes by the metal-alkyl hydroperoxide complexes in equation 11.
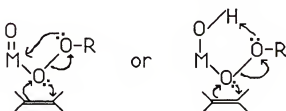
(11)

These mechanisms are also favored because they explain the epoxidation of allylic alcohols coordinated through their hydroxyl groups[59] better than the Mimoun mechanism. Mechanisms which bind the peroxide to the metal, through the oxygen atom adjacent to the alkyl group, can be discounted
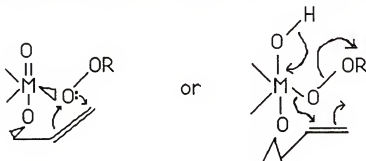
(12)

because the recent isolation of metal-alkyl hydroperoxide complexes by Mimoun and coworkers[63,64] provides sufficient evidence that the peroxide is coordinated to the metal through the distal oxygen. Mimoun has also demonstrated that the isolated metal-alkyl hydroperoxide complex is a selective catalyst for the epoxidation of alkenes.[64]

The oxidation of 2,4,4-trimethyl-1-pentene by t-butyl hydroperoxide with metal catalysts yields the epoxide in 100% selectivity for chromium, vanadium and molybdenum acetylacetonate catalysts.[65] The absolute yield of product is highest when molybdenum or vanadium catalysts are used. The epoxidation is also stereospecific with trans-4-methyl-2-pentene yielding exclusively the trans epoxide. Similarly, cis-4-methyl-2-pentene yields the cis epoxide exclusively. The hydroperoxide alone did not epoxidize the alkenes.[65] The reactions are very slow at 25°C, taking from four to seven days to reach completion. The reaction with $MoO_2(acac)_2$ (acac = acetylacetonate) performed at 60°C took four days to complete.

The oxidation of cyclohexene by alkyl hydroperoxides with molybdate catalysts (MoO_3, $CoMoO_4$, $MnMoO_4$ and Ag_2MoO_4) produces the epoxide in no greater than 50% yield for oxidations at 60°C. The other 50% of the products were 1-cyclohexen-3-ol and 1-cyclohexen-3-one in differing ratios, depending upon which catalyst was used.[66]

The transisiton-metal catalysts can catalyze the homolytic decomposition of the peroxide, leading to low epoxide yields, particularly at high hydroperoxide-to-olefin ratios.[67] BaO was added to stabilize the peroxides and this greatly increased the yield in the oxidation of organic substrates with alkyl

hydroperoxides.

The stereospecific[68,69] and enantioselective oxidation of alkenes by alkyl hydroperoxides is well explored in the literature. The oxidation of dienes by organic hydroperoxides with $Mo(CO)_6$ demonstrates that the epoxidation of nonconjugated alkenes is selective for the most substituted double bond.[70] Alpha,beta-unsaturated acids can be selectively epoxidized with tungstates and hydrogen peroxide.[71] Others have reported that the steroselectivity of the epoxidation depends upon the degree to which the double bond is shielded in the oxidation of delta-3 and delta-4-carenes by t-amyl-hydroperoxide in the presence of $Mo(CO)_6$.[68]

In order to further increase the stereoselectivity of the epoxidation of olefins by hydroperoxides, the catalysts and the substrates have been tailored to enhance the selectivity. The oxidation of steroids by the addition of a template molecule (an acetophenone acid-chloride with a tertiary alcohol in the para position) to the substrate is a very precise method for selectively oxidizing steroids. The reaction begins with the complexation of the molybdenum catalyst to the template hydroxyl. A template with the correct geometry is necessary for oxidation because small changes in the template structure diminish selectivity. Attack by uncomplexed reagent and intermolecular reaction are negligible under the described conditions.[72] The ability of the template molecule to direct oxidation has also been demonstrated for flexible polyenes such as trans-farnesol.[73]

The heterolytic and homolytic oxygen-transfer from stable metal-alkyl hydroperoxides has been studied by Mimoun and coworkers[63,64,74] for the

stereoselective oxidation of alkenes. The heterolytic or homolytic dissociation mode of the metal-peroxide controls the nature of the catalytic oxidation.[74] The isolation of a vanadium(V) alkylperoxidic complex with a Schiff-base ligand[64] yields an excellent catalyst for the selective epoxidation of cyclohexene to 1,2-epoxycyclohexane. It is also a stereoselective oxidant because, when cis-2-butene is oxidized, cis-2,3-epoxybutane is the sole product.[64] The CoBPI [BPI = 1,3-bis(2'-pyridylamino)indoline] alkyl-peroxy complexes are able to oxidize alkanes to ketones and alcohol.[63]

While much work has been done on the formation of stereospecific products by oxidation, very little successful work has been done in the field of asymmetric epoxidations. The asymmetric epoxidation of mono-substituted and alpha,alpha-disubstituted olefins has been performed with optically active peroxy acids.[75-78] (+)- Peroxycamphoric acid is the most commonly used peroxy acid in these epoxidation. Other reactions used optically active oxosulfonium ylides with aldehydes and ketones to produce oxiranes with yields from 7 to 43%.[79] The epoxidation of chalcone to optically active epoxides with quaternary salts of quinine (R1 = $C_6H_5CH_2$) by phase transfer of 30% hydrogen peroxide that is 2.0M in NaOH has also been reported.[80] This generated 99% optically active epoxide with an enantiomeric excess (ee) of 25%. Although the methods described above produce high yields of optically active epoxides, the optically active peroxyacids are difficult to generate and do not give 100%ee products. The oxidation with quaternary ammonium salts and hydrogen peroxide is the only reaction discussed that is catalytic and it does not generate more than a 25%ee.

The catalytic asymmetric epoxidation of alkenes to chiral epoxides in large ee has proven very difficult. The use of allylic alcohols as substrates, however, has greatly increased the ability of metal-alkyl hydroperoxides to selectively epoxidize alkenes. Vanadium catalysts have high yields of epoxides and faster rates of reaction when used for the oxidation of allyl alcohols.[70] Relative to the alkenes,[81-83] the allylic alcohols also exhibited greater stereoselectivity and regio-selectivity for their epoxidation with vanadium catalysts. The oxidation of allylic alcohols yielded stereoselective products with a large erythro-epoxy alcohol to threo-epoxy alcohol ratio.[83,84] For the oxidation of the geraniol and genaryl acetate,[82] peracids preferentially epoxidized the allylic alcohols at the double bond furthest from the alcohol. The acceleration in the rate and the high regioselectivity of the reaction suggests a mechanism in which the alcohol is coordinated to the metal in the rate-determining step.[70,82]

The synthesis of chiral molybdenum[85] and vanadium[59] catalysts for the epoxidation of allylic alcohols introduced a new method for the asymmetric epoxidation of alkenes. The allylic alcohols coordinate to the molybdenum and vanadium catalysts and they are epoxidized to their optically active, epoxy alcohols. The molybdenum complex uses a fixed chiral ligand [(-)-N-alkylephedrine] with acac as the removable ligand, because MoO_2acac_2 is a catalyst for the epoxidation of olefins.[85] This catalyst produced better optical yields (max 33%ee) than did the peroxyacids.[79,80] The vanadium catalyst[59] is generated in situ from $VO(acac)_2$ and chiral hydroxamic acids. Enantiomeric excesses up to 50% are observed for this catalyst. The $MoO_2(hydroxamate)_2$ catalysts, prepared prior to the reaction, generated no more than 2% asymmetric induction.

When Sharpless changed the chiral metal complex from a vanadium hydroxamate to a titanium [titanium tetraisopropoxide (+ or - diethyl tartrate), t-butyl hydroperoxide] catalyst system, the ee of the chiral epoxides increased dramatically at -23°C.[86-92] The less than 50%ee observed for the vanadium hydroxamate increased to more than 90%ee for the epoxidation of allylic alcohols. Exposure of the epoxides to the $Ti(isopropoxide)_4$ catalyst at room temperature or above caused the rearrangement of the epoxy alcohols to their diols.[86]

The highly enantioselective (>90%ee) epoxidation of allylic alcohols to their epoxy alcohols can be used to sythesize useful compounds such as erythromycin[87] and for the kinetic resolution of racemic allylic alcohols.[88] The latter is performed by increasing or decreasing the rate of oxidation. The epoxidation of the (S)-enantiomer is 98% selective for the erythro enantiomer at rapid rates of reaction. The asymmetric epoxidation of the (R)-enantiomer is far slower and only 62% selective for the erythro epoxy alcohol.[88]

Yields from the asymmetric epoxidation of allylic alcohols are generally low. The addition of molecular sieves to the reaction leads, however, to high conversion (>95%) and high enantioselectivity (90-95%ee).[89]

The titanium diethyl tartrate catalysts have also been used with t-butyl hydroperoxide for the synthesis of chloro diols from allylic alcohols with $TiCl_2(isopropoxide)_2$ as the catalyst precursor.[90] $TiCl_4$ has been used for the chlorohydroxylation of olefins.[93] These two reactions probably proceed by a mechanism in which the formation of an epoxide is followed by decomposition of the epoxide to the chloro alcohol.[91,93] This mechanistic pathway is

supported by work on the titanium-catalyst-mediated nucleophilic ring opening of 2,3-epoxy alcohols. It has been demonstrated that the epoxide ring could be selectively opened to form the diol in the presence of a nucleophilic amine.[94,95] This catalyst can also be used for the enantioselective oxidation of beta-hydroxy tertiary amines.[96]

We chose to try several catalysts which seemed promising for the epoxidation of alkenes and several literature catalysts for the oxidation of olefins with alkyl hydroperoxides. The catalysts that were used are as listed: heteropolyanions, porphyrins, molybdenum complexes, CoBPI and cyano cobalt(II) in a Y zeolite.

The heteropolyanions were good potential catalysts for the oxidation of alkenes because they have high initial oxidation states and because the heteropoly blues have several reduced oxidation states available to them. The heteropolytungstates were the most likely candidates for catalytic activity, given that Hill[97] and others have classified the heteropolytungstates and the heteropolyvanadates as type III heteropolyanions. The type III heteropolyanions are the only heteropolyanions which can be reoxidized to their highest oxidation state by oxygen, alkylhydroperoxides or iodosylbenzene. The heteropolymolybdates are not easily reoxidized to their highest oxidation states by these three common oxidizing agents. They are, however, powerful oxidizing agents, capable of oxidizing substrates that the heteropolytungstates cannot. Our goal in this research was to find heteropolyanions which would oxidize alkenes with readily available oxidizing agents such as those listed above. Hill has already demonstrated that heteropolytungstates will rapidly

oxidize alkenes in the presence of iodosylbenzene.[98] Trost has shown that the molybdates will oxidize organic substrates with hydrogen peroxide.[99] These experiments led us to believe that phase-transferred heteropolyanions would make excellent homogeneous catalysts for the oxidation of alkenes.

Heteropolyanions and isopolyanions make up a large group of polynuclear oxocomplexes of the transition metals of group VB and VIB. Isopolyanions contain a number of atoms of the same metal (V,Nb,Ta,Mo,W), linked by bridging oxygen atoms to form a "continuous polytungstate or polymolybdate 'ligand.'"[100] This structure is made up of MO_6 units which share oxygen atoms and contain one or two terminal oxygen atoms. The Anderson structures (figure 3-1) have two terminal oxygen atoms and four bridging oxygen atoms per metal MO_6 unit. The more common Keggin-type structure (figure 3-2) contains one terminal oxygen and five bridging oxygen atoms per MO_6 unit as does the $XMo_9O_{32}^{6-}$ type structure (figure 3-3).

If the anion contains an atom dissimilar from the structural metal atoms, it is called a heteropolyanion.[101] Heteropolyanions incorporate two different types of heteroatoms: primary and secondary.[100] Primary heteroatoms are essential to the heteropolyanion structure and in the Anderson and Keggin-type structures occupy the central position in the heteropolyanion. The primary heteroatom shares at least one oxygen atom with each MO_6 unit in the Anderson structure and in the $XMo_9O_{32}^{n-}$.[100] Secondary heteroatoms occupy peripheral positions in the heteropolyanion structure by replacing one of the Group VB or VIB structural MO_6 groups which previously occupied that position.[102]
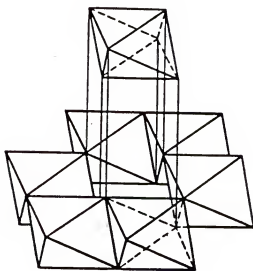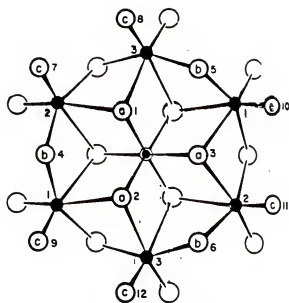
Figure 3-1   Anderson-type Structure, $[CrMo_6O_{24}H_6]^{3-}$
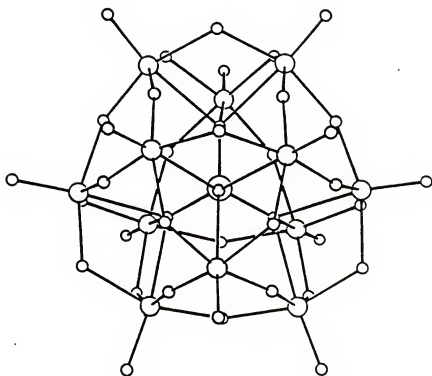
Figure 3-2   Keggin-type Structure, [PW12O40]3-
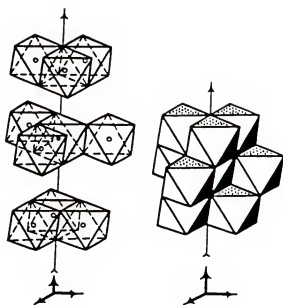
Figure 3-3   Structure of MnMo$_9$O$_{32}^{6-}$

The most common heteropolyanion structure found in the literature for tetrahedral primary heteroatoms is the Keggin-type structure of the $XM_{12}O_{40}^{n-}$ (M = Mo, V or W) anion. These contain a tetrahedral central heteroatom and can undergo further substitution through the formation of lacunary ions of the form $XM_{11}O_{39}^{n-}$, following the loss of a MO^{n+} group from the Keggin-type anion. The lacunary anions can then replace the lost MOn+ group with a heteroatom at a secondary site to form $XAM_{11}O_{39}^{n-}$ heteropolyanion. It is possible to build a metal ligand around the heteroatom of choice by replacing one of the secondary atoms of the heteropolyanion with a heteroatom. We should be able to do catalytic chemistry with heteropolyanions similar to that of porphyrins without having the highly oxidizable porphyrin ring present. Pope has recently found that solutions of phase-transferred $[Cr(OH_2)SiMo_{11}O_{39}]^{5-}$ will react with iodosylbenzene in organic solvent to form the chromium(V) species: $[CrOSiMo_{11}O_{39}]^{5-}$. This clearly indicates that heteropolyanions will react in the same way with iodosylbenzene as do porphyrins.[103] This data, coupled with the fact that the $[Mn(II)SiW_{11}O_{39}]^{6-}$ can be oxidized to $[Mn(III)SiW_{11}O_{39}]^{5-}$ with oxygen at low temperatures,[104] indicates that heteropolyanions should be good alternatives to porphyrin type catalysts. They are not susceptible to oxidative degradation and seem to have oxidative activity similar to that of the porphyrin catalysts. The asymmetric $XMo_9O_{32}^{6-}$ anion has a primary MO_6[M = Mn(IV) or Ni(IV)] unit with an asymmetric arrangement of nine MoO_6 units around it.[100] The ammonium salts of the $MnMo_9O_{32}^{6-}$ anion can be isolated as orange-red crystals. This heteropolyanion obviously does not oxidize substrates in the same way as the heteropolyanions containing

secondary heteroatoms. The heteropolyanions containing secondary heteroatoms can react directly at the surface of the heteropolyanion. The Mn(IV) is not accessible to substrate, and any oxidations by this heteropolyanion must proceed through an outer-sphere mechanism in which the central heteroatom, rather than the structural molybdates, is reduced. This has been demonstrated for the $[Co(III)W_{12}O_{40}]^{5-}$ heteropolyanion in the literature.[105]

Solid molybdates have been used for a number of years in the commercial process: for the oxidation of propylene over bismuth molybdates, for the production of acrolein with air and water, and for the ammoxidation of propylene to acrylonitrile with air and ammonia. The Shell catalyst is a heterogeneous system in which the amorphous bismuth molybdate lies in a fixed bed reactor and the substrate is passed over the catalyst at elevated temperatures.[43-46] Following this discovery, a number of groups began exploring the tungstates, vanadates and the molybdates as potential catalysts for the oxidation of olefins and alkylaromatics.

Most of the recent work with the molybdate, tungstate and vanadate catalysts has been performed in homogeneous systems, using solubilized heteropolyanions. There have been problems in obtaining an active heteropolyanion oxidation system because heteropolyanions are very soluble only in water. Polymeric molybdates, tungstates and vanadates as well as discrete heteropolyanions have been solvated by a variety of methods in order to circumvent this problem.

Trost has shown that the polymeric molybdate, ammonium paramolybdate,

dissolved in either THF or DMF will oxidize alkenes in the presence of hydrogen peroxide.[99] Trost was able to epoxidize cyclooctene to 1,2-epoxycyclooctane in 75% yield, using 30% aqueous hydrogen peroxide which was phase transferred by tetrabutylammonium chloride into the organic solvent and catalyzed by ammonium paramolybdate. Trost found that cyclic 1,2-disubstituted olefins and allylic alcohols were very reactive substrates in this catalyst system. The cyclic olefins were epoxidized and the allylic alcohols were oxidized to their allylic ketones or their epoxides.[99] Heteropolyanions are either made in their acid form or as alkylammonium salts for use as homogeneous catalysts in organic solvents.[98,106,107] The acid heteropolyanions have been used in the photochemical dehydrogenation of alkanes by Hill.[97,108] The quaternary ammonium salts are susceptible to photooxidation by the heteropolyanions and cannot be used successfully for photochemical experiments with heteropolyanions.[98] The acid heteropolyanions are also soluble in some organic solvents and have been used for catalytic photochemistry without the loss of the heteropolyanion structure.[108]

The quaternary ammonium salts of the heteropolytungstates, $HMPW_{11}O_{39}^{4-}$ [where M= Mn(II) or Co(II)], are used for the oxidation of olefins with iodosylarenes. In addition to their stability in the presence of a strong oxidant, the selectivity for epoxides in the oxidation of olefins is greater than ninety percent.[98]

The cyano cobalt(II) Y zeolite catalyst $[Co(CN)_x\text{-NaY}]$ used in the oxidation of alkenes is believed to contain a tetracyano cobalt(III) dioxygen adduct.[109]

Square planar complexes of $Co(CN)_4^{2-}$ have been isolated in the literature[110] and cobalt amine oxygen adducts have been observed in the Y zeolite.[111,112]

The structure of the Y zeolite (shown in figure 3-4), with its large openings (12-ring aperture is 7.4A in diameter with an 8.1A kinetic diameter) into the large supercage (13A diameter),[113] is excellent for the synthesis of metal complexes for catalysis.[114-116] The zeolites without adsorbed metal complexes are also good catalysts for organic synthesis.[117] Their activity and selectivity is greatly increased, however, by the addition of metal complexes.[118]

The disproportionation of nitric oxide on Y zeolites[119] and the reduction of nitric oxide by ammonia over cobalt-exchanged[120] and cobalt-amine exchanged[121] NaY zeolite have been reported in the literature. The reaction between Co(II)-, Fe(II)-, Cr(II)-, Ni(II)- and Ag(I)-exchanged NaY zeolites with nitric oxide, forming metal-nitrosyls in the NaY zeolite, has also been explored.[122-126] With 85% selectivity for acetone and 2.5 turnovers (molecules acetone/Co(II) atom) per cobalt, the oxidation of 2-propanol to acetone can be performed with cobalt dinitrosyl complex in the Y zeolite. NO, O_2 and 2-propanol are passed through the Co-Y zeolite in a flow reactor at 70°C.[127] The catalytic abilities of the other metal nitrosyl complexes have not been explored because the reduced cobalt-nitrosyl catalyst cannot be regenerated rapidly by molecular oxygen.

The shape-selective oxidation of alkanes by Fe(II) and Pd(0), dispersed in a 5A zeolite, has been performed under an atmosphere of H_2 and O_2 at 25°C.[128] The octane/cyclohexane selectivity is greater than 190 and the primary/secondary regioselectivity is 0.67 after the surface iron(II) has been
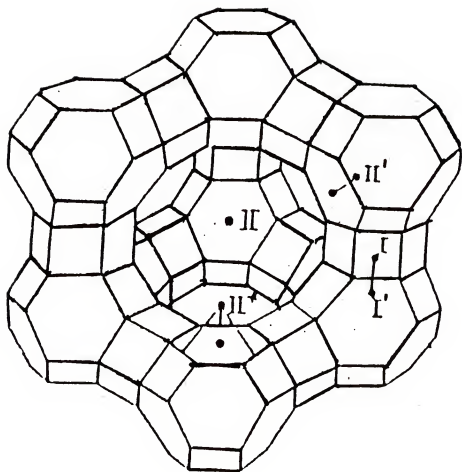
Figure 3-4   Zeolite Y

poisoned with 2,2-bipyridine. Highly selective oxidations by a nonselective oxidant are performed by placing the catalyst in the shape-selective environ of the 5A zeolite. The products are difficult to remove from the 5A zeolite and currently Tolman and Herron are using mordenite rather than the 5A zeolite for these oxidations.[129] Mordenite has larger apertures than the 5A zeolite and this allows the product to exit from the zeolite.

The metalloporphyrin catalysts have been used successfully in the selective oxidation of alkenes and alkanes. They successfully imitate the activity of cytochrome P-450 which hydroxylates a variety of substrates and metabolizes various compounds, including drugs.[130] The first complexes to successfully bind oxygen were the "picket-fence porphyrins" of Collman.[131,132] The 5, 10, 15, 20-tetraphenyl-21H,23H-porphyrins (TPP) are the most commonly used porphyrins for the oxidation of organic substrates. Fe(II) and Mn(II) are the most common metals exchanged into the TPP. The Fe(IV) porphyrins are proposed to contain the ferryl group[133-136] $(Fe^{IV}=O)^{2+}$ which is the active species for the oxidation of olefins.[137-140] The ferryl species is difficult to form with the TPP ligand because it tends to dimerize to the peroxy-bridged metalloporphyrin complex.[141,142] The dimerization problems in the Fe(III) oxoporphyrins require that either the phenyl groups of the porphyrin are replaced with bulkier ligands, such as mesitylene,[138,139] or that nitrogen bases are added to stabilize the monomer.[140]

The iron and manganese porphyrins have been used with a large number of oxidants for the oxidation of alkenes. Peroxyacids,[143] molecular oxygen,[144] NaOCl,[145-154] iodosylbenzene,[156-166] amine oxides[167-170] and alkyl

hydroperoxides[171-174] are all used for the oxidation of alkenes and alkanes by metalloporphyrins to their epoxides, alcohols and ketones.

It has been proposed that the mechanisms for the oxidation of alkenes and alkanes by iodosylbenzene and hypochlorite follow a mechanism in which the active species is a ferryl group or its equivalent.[152,172]

The characteristics of the alkyl-hydroperoxide oxidations with metalloporphyrins unfortunately indicate that the oxidation of alkanes is independent of the type of metal used in the porphyrin. Mansuy and coworkers propose that these peroxide oxidations follow a "Fenton-type" mechanism in which an alkoxy radical is formed by the mechanism shown below.[172]

$$M^n(P) + CumOOH \longrightarrow (P)M^{n+1}-OH + CumO\bullet$$

$$\xrightarrow[-CumOH]{+RH} R\bullet + (P)M^{n+1}-OH \longrightarrow ROH + M^n(P)$$

$$\text{(13)}$$
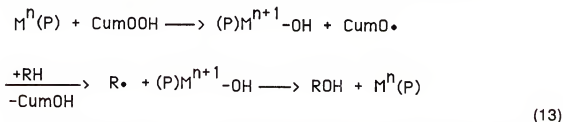
One would expect that the peroxide/metalloporphyrin system is unable to epoxidize olefins based on this mechanism and this is true for cyclohexene[154] and 1-hexene.[172]

It has recently been demonstrated by Valentine and coworkers that simple metal salts, including those of copper[175,176] and the binuclear Cu(II) complexes of Karlin[177-179] were capable of epoxidizing olefins with iodosylbenzene. It appears that the formation of a metal oxide similar to the ferryl group does not occur, but that a copper-iodosylbenzene complex is formed instead.[177] The copper-iodosylbenzene is capable of oxidizing alkenes just as well as the ferryl type mechanisms. The mechanism for this

reaction is expected to be similar to that for the metal alkyl peroxide mechanisms described by Sharpliss and Mimoun.

Materials

Y-52 zeolite from Union Carbide (lot No. 9680-84-61002) was prepared for use by stirring the zeolite in a 0.25M NaCl solution for four hours to ensure that all counter-cations would be completely exchanged for sodium. The NaY zeolite was washed on a frit with two liters of deionized water, thereby removing the excess sodium. The filtrate was then tested for chloride with silver nitrate after several washings. Following the washing, the NaY zeolite was dried in vacuo at 150°C.

The alkene substrates were passed through a column of activated alumina immediately before use in order to remove all peroxides. The alkenes and their oxides were readily available.

The 1-methyl-2-pyrrolidinone was HPLC grade from Aldrich and was used as received. Gas chromatography and NMR indicated that the HPLC grade 1-methyl-2-pyrrolidinone did not contain any detectable impurities. Iodine titration of the 1-methyl-2-pyrrolidinone did not detect any peroxides in the starting material.

The methyltrioctylammonium bromide (MTOABr) was acquired from Fluka A.G. and used as received. t-Butyl hydroperoxide was purchased from Aldrich as an anhydrous 3M solution in toluene and was used as received. The toluene (Fisher) and the anhydrous t-butyl hydroperoxide solution in toluene

showed no traces of benzaldehyde prior to use. All materials for the synthesis of the heteropolyanions were readily available and were used as received, except the $RuCl_3 \cdot 3H_2O$, which was purified by a literature method.[180] Other materials were purified as described. Deionized water was used in all synthesis and in the phase-transfer of the heteropolyanions.

Methods

The acetonitrile, used for cyclic voltammetry, was dried over 3A sieves (5% w/v) for one week, filtered and placed over fresh sieves for 24 hours. After removing the acetonitrile from the molecular sieves, the dry acetonitrile was stored over 3A sieves until it was used. Prior to use, the 3A molecular sieves were activated under flowing nitrogen from 250 to 320°C overnight.[181,182]

All electrochemical measurements were made in acetonitrile with either 0.1M tetrabutyl ammonium tetrafluoroborate or 0.1M tetrabutyl ammonium perchlorate electrolyte. The heteropolyanion solution was purged with Argon for 5 to 10 minutes prior to measurement. The cyclic voltammetry was performed with an EG & G PARC Model 175 Universal programmer and an EG & G PARC 173 Potentiostat/Galvanostat. The voltammograms were recorded on a Houston Instruments X-Y Omnigraphic 2000 recorder. A platinum button, Ag/AgCl-saturated KCl, and a platinum wire were used as working, reference, and counter-electrode respectively.

Ultraviolet and visible spectra were recorded on a Perkin-Elmer 330 spectrophotometer in 1cm path length quartz cells. Infrared spectra were recorded on a Nicolet 5DXB FTIR spectrophotometer in nujol on NaCl salt

plates, as powders in KBr, using a diffuse reflectance apparatus, or in NaCl window solution cells. Water analysis was performed on a Perkin-Elmer 7 Series Thermal-Analysis System. The typical onset for loss of H_2O from the heteropolyanions was approximately 50 to 100°C with endpoints near 200°C.

The heteropolyanions were analyzed for their metal content (P, Si, Co, Mn, Fe, Mo and W) on a Perkin-Elmer ICP Plasma II emission spectrometer in either 10% by volume concentrated HCl or in 1M NaOH.

The heteropolyanion was phase-transferred from aqueous solution into toluene by using the alkylammonium salts: tetraheptylammonium bromide and methyltrioctylammonium bromide.
Approximately 0.5g heteropolyanion (6×10^{-4} moles) was disolved in 20ml water with vigorous stirring at room temperature, and 1.0g of the alkylammonium bromide (2×10^{-3} moles) was dissolved in 20ml toluene. The aqueous heteropolyanion and the phase-transfer agent dissolved in toluene were stirred together vigorously until the aqueous phase was decolorized. The toluene was then separated from the aqueous layer and was either used directly for oxidations or rotovapped, yielding the alkylammonium salt of the heteropolyanion.

The phase-transferred heteropolyanion was then mixed with the t-butyl-hydroperoxide (in toluene solvent) and diluted to 25ml with toluene. 2-hexanone (1ml) was added as an internal standard for GC analysis. The oxidations were performed with vigorous stirring in 50ml roundbottom flasks covered by rubber septa. The flasks were heated in a constant-temperature oil bath during the reaction time period. One ml samples were taken periodically

for GC analysis. The oxidations, under 10 to 20 psig O_2 pressure, were performed in a 250ml Parr pressure apparatus (figure 2-1), which was sampled by syringe (12 inch, 20 gauge needle). All other reactions were performed at $75^{\circ}C$ under 50 psig oxygen, unless indicated otherwise.

Gas chromatograms were obtained on a Varian 3700 GC, equipped with a flame ionization detector (FID), and a Hewlett-Packard 3390A integrator, for the oxidation of toluene and butyl sulfide. Toluene products were separated on an eight foot, 1/8 inch O.D., stainless steel column packed with 5% diethylene glycol adipate, supported on 80/100 mesh chromasorb P. Butyl sulfide products were separated on a 6 foot, 1/8 inch O.D., stainless steel, carbowax column. All products were identified and quantified, using known standards.

The oxidation of cyclohexene, 1-hexene, trans-beta-methylstyrene and butyl sulfide were performed in a Parr pressure bottle (figure 2-1) in 50ml of 1-methyl 2-pyrrolidinone. In a typical experiment, 1 to 3 ml of the substrate and 0.5ml of an internal standard (cyclooctane or 2-octanone) were diluted to 50ml with 1-methyl-2-pyrrolidinone. The solution was mixed with 30 to 100mg of catalyst in a Parr pressure bottle. The Parr pressure bottle was purged three times with oxygen and pressurized to 50 psig with oxygen and placed in an oil bath at $75^{\circ}C$. Unless noted otherwise, all oxidations were performed at $75^{\circ}C$ under 50 psig oxygen. The sampling for GC analysis performed by previously described methods.

Gas chromatography of the cyclohexene, 1-hexene and trans-beta methylstyrene oxidation products was performed on a Varian 3300 GC with an FID on a six-foot, stainless steel, DEGS column. All products were identified

and quantified using known standards. For all oxidations, the FID detectors were calibrated with known quantities of standard solutions.

The epr were performed on a Bruker 200D-SRC instrument with a Bruker ER 040 XR microwave bridge. GC-MS and NMR were performed as described previously.

The analysis of the Co-Y and $Co(CN)_x$-NaY catalysts was performed after letting the samples sit in a wet dessicator for 24 to 48 hours, so that the zeolite would absorb its maximum number of waters of hydration. The wet samples were placed on a bench top, opened to the air, so that they would come to equilibrium and not change weight during analysis. The sample for carbon, hydrogen and nitrogen (CHN) analysis was removed and sealed in a vial. The remainder was similarly sealed in a vial prior to analysis for cobalt.

CHN analysis of the $Co(CN)_x$-NaY catalysts was performed on a service basis by the Microanalytical Lab at the University of Florida.

Cobalt analysis was performed by weighing out approximately 0.1g of the wet $Co(CN)_x$-NaY and slurrying it in 5ml of 6M HCl with 10ml of deionized water. The samples were refluxed for several hours. After the refluxing, 10ml of 6M NaOH and 15ml of 0.2M Na_4EDTA were added to the sample, which was refluxed again. To remove the Y zeolite after refluxing, the samples were filtered, while still hot, through Whatman No. 1 filter paper . One ml of hydrogen peroxide was added to the filtrate before it was diluted to 100ml with deionized water. Three to four samples of each $Co(CN)_x$-NaY catalyst were prepared in this manner for analysis on the Perkin-Elmer ICP Plasma II emission spectrometer. Standards were prepared in the same manner as the samples.

The analysis for "free Co^{II}" was carried out in a similar manner. 100mg of the Co(CN)$_x$-NaY was slurried with 25ml of 0.2M Na$_4$EDTA for 10 to 12 hours at 60 to 70°C. The samples were filtered into 100ml volumetric flasks and 0.5ml of 3% H$_2$O$_2$ was added to them. The solutions were diluted to 100ml with deionized water and analyzed on the Perkin-Elmer ICP Plasma II emission spectrometer.

Catalyst Synthesis

Sodium 6-molybochromate(III)   Na$_3$[CrMo$_6$O$_{24}$H$_6$]·7H$_2$O

The sodium salt was prepared using Perloff's method.[183] The crystalline product was dried overnight in vacuo at 60°C. The loss of a water of hydration from the heteropolyanion destroyed its crystallinity, yielding a pink powder.

Elemental Analysis:

	%Cr	%Mo	%H$_2$O
Calculated	4.29	47.49	10.39
Measured	4.30	47.58	9.49

Ammonium 9-molybdomanganate(IV)   (NH$_4$)$_6$[MnMo$_9$O$_{32}$]

Ammonium 9-molybdomanganate(IV) was prepared according to Baker and Weakley's method.[184] When dissolved in water, the UV-Vis spectrum of the orange-red crystals matched the literature spectrum.[185] The epr of the Ammonium 9-molybdomanganate(IV) anion has a broad signal with a g-value

of approximately 3.7. Typical g-values for manganese(IV) compounds are near 3.8.

Elemental Analysis:

	%Mn	%Mo
calculated	3.57	56.14
measured	3.53	56.51

Ammonium 6-molybdoiron(III) $(NH_4)_3[FeO_6Mo_6O_{15}] \cdot 10H_2O$

Ammonium 6-molybdoiron(III) was made using Baker's method. The product of this reaction was a yellow powder, not the white four sided plates which Baker had described in his synthesis.[186]

Elemental Analysis:
(not performed, due to the heteropolyanions insolubility in either acidic or basic solution)

Ammonium 12-tungstodicobaltoate $(NH_4)_8[Co^{II}Co^{II}W_{12}O_{42}] \cdot 20H_2O$

The ammonium 12-tungstodicobaltoate was synthesized using Baker and McCutcheon's method.[187]

Elemental Analysis:
(The ammonium 12-tungstodicobaltoate was not analyzed because it is for all practical purposes, insoluble in aqueous solution.)

<u>Ammonium 6-molybdochromium(III)</u> $(NH_4)_3[CrMo_6O_{24}H_6]\cdot7H_2O$

Synthesis of the ammonium 6-molybdochromium(III) was accomplished by altering a preparation from the literature originally intended for use in the synthesis of the sodium salt.[183] Ammonium molybdate was substituted for sodium molybdate dihydrate in the prep. The pink powder product was recrystallized in hot water to yield the final product.

Elemental Analysis:

	%Cr	%Mo	%H2O
calculated	4.34	48.08	10.52
measured	4.27	48.01	13.08

<u>Alpha-11-tungstosilicate</u> $K_8[SiW_{11}O_{39}]\cdot12H_2O$

Alpha-11-tungstosilicate dodecahydrate was synthesized according to literature methods,[188] and was used in all syntheses requiring the lacunary ion ($SiW_{11}O_{39}{}^{8-}$), except where noted.

<u>Potassium 11-tungstosilicate iron(III)</u> $K_5[Fe(OH_2)SiW_{11}O_{39}]\cdot11H_2O$

The alpha-11-tungstosilicate which had been synthesized earlier by literature methods was used for the synthesis of the $SiFe(OH_2)W_{11}O_{39}{}^{5-}$ heteropolyanion, according to the Tourne preparation.[188] Two crystalline products were obtained from this procedure: one, a light yellow and the other, a yellow-green. The yellow-green heteropolyanion is most likely contaminated

with excess iron(III), present as the counterion to the heteropolyanion. Only the yellow heteropolyanion was used for analysis, electrochemistry and reaction.

Elemental Analysis:

	%Si	%Fe	%W	%H2O
calculated	0.89	1.78	64.38	6.30
measured	0.39	0.97	64.30	2.84

<u>Potassium 11-tungstophosphate manganese(II)</u> $K_5[MnPW_{11}O_{39}] \cdot 14H_2O$

This heteropolyanion was synthesized using the Weakley method for the synthesis of the $NiPW_{11}O_{39}^{5-}$ salt.[189] Bailar's method[190] for the preparation of 12-phosphotungstic acid was followed at one-tenth scale until the separation of the etherate layer from the aqueous and ether phases. From this point on, the synthesis was performed in accordance with Weakley's preparation for anion VI .[189] The etherate was diluted with 200ml of water and heated to 90°C (If bluish in color, one or two drops of bromine water were added to remove the color.), then 5.45g of $MnCl_2 \cdot 4H_2O$ and 80g of potassium acetate in 80ml of hot water (pH adjusted to 7) were added.

This mixture was heated to 90°C for two minutes, filtered rapidly at 90°C and cooled down to 60°C. At this point, an equivalent volume of methanol was added to the solution. This was then filtered again to remove brown MnO_2 and other insoluble species. The solution was refrigerated overnight and filtered at low temperature. The product was an orange-yellow powder. The powder was recrystallized twice in water at 60°C.

Elemental Analysis:

	%Mn	%P	%W	%H2O
calculated	1.72	0.97	63.25	7.88
measured	1.41	0.89	63.06	5.61

<u>12-Molybdophosphoric acid</u> $H_3PW_{12}O_{40} \cdot 14H_2O$
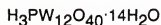
12-molybdophosphoric acid was prepared using Tsigdinos' method.[191] The product was yellow crystalline material which slowly effluoresced to give a yellow powder. Extensive exposure to air and light turned the yellow powder to a light blue. This discoloration was removed by adding one or two drops of bromine water to a hot aqueous solution of the product heteropolyanion.

Elemental Analysis:

	%P	%Mo	%H2O
calculated	1.49	55.41	12.14
measured	1.96	52.91	6.81

<u>Potassium 11-tungstosilicate cobalt (II)</u> $K_6[CoSiW_{11}O_{40}H_2] \cdot 12H_2O$

This heteropolyanion was produced using Malik and Weakley's[189] method for the preparation of anion I. After the first precipitate (a reddish powder) formed, it was dissolved in approximately 20ml of hot water, boiled, filtered and put into a refrigerator. Dark red crystals of the potassium salt of the $CoSiW_{11}O_{40}H_2^{6-}$ anion were obtained when this procedure was repeated

once more. The cobalt (II) heteropolyanion was not oxidized to the cobalt(III)

heteropolyanion.

Elemental Analysis:

	%Si	%Co	%W	%H_2O
calculated	0.88	1.84	63.17	6.75
measured	0.59	1.29	61.12	6.48

Alkylammonium 11-tungstogermanate ruthenium(III)

0.5g GeO_2, 10ml of 5% NaOH in water, 17g of Na_2WO_4-$2H_2O$ and 40ml of

hot water were placed in a 500ml roundbottom flask and stirred at 90°C. 10ml

of concentrated HCl were added dropwise. The solution was heated for an

additional two hours and then allowed to cool to room temperature.

15ml of diethyl ether and 10ml of concentrated HCl were added to the aqueous

solution. The etherate layer was removed in a separatory funnel and 40ml of

water was added to the etherate. The ether was boiled off at 77°C in one-half

hour. 1.31g of $RuCl_3$-$3H_2O$ in 10ml hot water was added to the

11-tungstogermanate solution and this mixture was stirred for one hour. 14.8g

of methyl trioctylammonium bromide, dissolved in 100ml toluene, was then

stirred into the solution for a few minutes.   Following a thorough mixing of the

two solutions, the mixture separated into three layers which were separated and

rotovapped. All three were dissolved in acetonitrile and filtered. The top two

layers were added together and rotovapped down again to yield a purple oil.

The bottom layer was a green-black oil.

Potassium 11-molybdophosphate rhodium(III)

The acid of 12-tungstophosphate was prepared according to Tsigdinos' method.[191] The 12-tungstophosphate acid was dissolved in hot water (90°C) and concentrated HCl was added until the pH was between 4.3 and 4.5.[194] An equimolar quantity of rhodium trichloride, dissolved in 10ml of water, was added to the hot 12-tungstophosphate solution. The solution was heated at 90°C for an additional half hour, then cooled to 50°C and filtered. An equal volume of ethanol was added to the solution and the mixture was passed through a column of Amberlite IR-120 cation exchanger in the potassium form, thus removing the cationic rhodium(III) contaminant.[193] The solution was then chromatographed on a 70-230 mesh silica gel column yielding both a green and a blue phase. Attempts to convert the blue phase into the green heteropolyanion with ceric ammonium nitrate did not succeed. The blue heteropolyanion instead formed a white precipitate when oxidized and the solution became colorless.

Alkylammonium 10+x-tungstogermanate bis-rhodium(III)

The synthesis of this heteropolyanion was performed by a technique similar to that published in the dissertation of a previous member of our research group, Ken Balkus.[194] 0.5g of germanium oxide was dissolved in 10ml of a 5% NaOH solution in a 250ml roundbottom flask and 17g of sodium tungstate, dissolved in 40ml of deionized water, was added to the flask. The contents were stirred at 90°C. 10ml of concentrated HCl was added dropwise and the

solution was heated for an additional hour with a reflux condenser.

After heating, the solution was cooled to room temperature and 20ml of diethyl ether was added to the solution. 10ml of concentrated HCl was added to form the etherate of the lacunary ion ($[GeW_{11}O_{39}]^{8-}$). The lower etherate layer was removed in a separatory funnel and poured into a 250ml roundbottom flask with 40 to 50ml of water. The solution was warmed at 70°C in order to drive off the ether and, after 1/2 hour, 1.32g of rhodium trichloride in 10ml of water was added to the lacunary ion solution. The solution was then stirred for an additional hour at 70°C before adding 13.5g of methyl trioctylammonium bromide in 40ml of hot water.

The green oil that formed upon the addition of the alkylammonium salt was isolated by vacuum filtration, dissolved in acetonitrile, filtered and rotovapped down to a viscous oil. The dark-green oil product was then vacuum-dried at 75°C in vacuo overnight yielding a dark-green viscous oil similar to that produced by Balkus.[194]

Molybdenum carbonyl $Mo(CO)_6$

Molybdenum carbonyl was used as received from Strem Chemical Co.

Cobalt octoate $Co(octoate)_2$

The $Co(octoate)_2$ (octoate = 2-ethylhexanoate) was purchased from Mooney as a 12% solution by weight of cobalt in mineral spirits.

Molybdenyl acetylacetonate $MoO_2(acac)_2$

Molybdenyl acetylacetonate was synthesized according to a literature

preparation.[195] The orange-brown solid was refluxed a second time with excess acetylacetonate and precipitated in order to purify it.

Vanadyl acetylacetonate   VO(acac)$_2$

VO(acac)$_2$ was obtained from another member of the Drago group and was used as received.

Tetraphenylporphine manganese(II) chloride   TPPMnCl

5, 10, 15, 20-tetrapheny-21H, 23H-porphine (TPP) was purified by a literature method to remove tetraphenyl chlorin.[196] The purified TPP was reacted with manganese(II) acetate tetrahydrate in DMF, yielding TPPMnCl by the method of Basolo.[197] The TPP[196] and the TPPMnCl[198] were identified by comparing their respective visible spectra to those reported in the literature.

The TPPMnCl was purified by recrystallization in CH$_2$Cl$_2$/hexanes by a literature method.[152]

Elemental Analysis:

	%C	%H	%N
calculated	75.16	4.01	7.94
found	75.36	4.01	7.97

<u>5.10.15.20-tetraperfluorophenylporphine iron(II) chloride</u> F_{20}TPPFeCl

   F_{20}TPPFeCl was purchased from Aldrich and purified by chromatography.[167]

<u>Cobalt(II) 1.3-bis(2-pyridylimino)isoindoline</u>   CoBPI

   CoBPI was synthesized from literature methods[199,200] by Curt Barnes and was used without further purification.

<u>Tetracyano nickel(II) Y zeolite</u>   Ni(CN)$_4$-NaY

   Ni(CN)$_4$-NaY was obtained from Robert Taylor Jr. and was used as received.

<u>Tetracyano cobalt(II) anion in NaY zeolite</u>

Ia   Co(CN)$_x$-NaY

   20g of the NaY zeolite was placed in 190ml of 0.4M CoCl$_2$·6H$_2$O aqueous solution and stirred at 70°C for 24 hours. The Co-Y zeolite was filtered and washed with water until the pink color, indicating the presence of excess cobalt, was removed from the filtrate. The Co-Y was then dried at 150°C overnight in a vacuum oven. 8g of the Co-Y made by this method was slurried in 400ml of dry methanol with 16g of NaCN at room temperature for five days with vigorous stirring. The Co(CN)$_x$-NaY was then filtered and washed exhaustively with methanol to remove all excess cyanide. The epr of this species gave a strong signal indicating the presence of the cyano cobalt(III) dioxygen adduct.

The epr of this species had the strongest epr signal indicating the presence of the cyano cobalt(III) dioxygen adduct.

Ib   Co(CN)$_x$-NaY

10g of the NaY zeolite was dissolved with 0.732g CoCl$_2 \cdot$H$_2$O in approximately 200ml of deionized water and stirred overnight at room temperature. The Co-Y was filtered, yielding a clear filtrate which indicated that all the cobalt was adsorbed into the NaY zeolite. The pink solid was dried at 150°C in vacuo overnight. The Co-Y was blue when dry. The dry Co-Y was slurried in 1300ml of methanol with 3g of dNaCN and stirred vigorously for four days. The solid was filtered off and washed with 300ml of methanol. The washed solid was then placed in a vacuum oven at 150°C overnight. The epr of Ib Co(CN)$_x$-NaY contained a small broad signal.

Ic Co(CN)$_x$-NaY

20g of NaY was slurried with 180ml of 0.4M CoCl$_2 \cdot$H$_2$O at 70°C for 24 hours. The solid was filtered and washed exhaustively with water until the solution was colorless and tested negative for chloride ion. It was then dried in a vacuum oven at 160°C.

8g of the dried Co-Y was placed in 400ml of methanol with 16g of NaCN and stirred vigorously for nine days. The solid was then filtered and washed repeatedly with methanol and dried at 150°C in vacuo. The epr of Ic Co(CN)$_x$-NaY contained virtually no epr signal, which indicated that there was very little of the cobalt(III) dioxygen adduct present.

Id   Co(CN)$_x$-NaY

0.75g of CoCl$_2$·H$_2$O was dissolved in 300ml of nanopure water and slurried with 10.06g of NaY zeolite overnight and filtered. The solid was not washed on the frit because the filtrate was clear. The clear filtrate indicated that all of the cobalt(II) had been adsorbed into the Y zeolite. The solid was heated in a vacuum oven at 150°C overnight and was mixed with 3g of NaCN in 600ml of dry methanol (stored over molecular sieves prior to use) while still hot. The slurry was stirred vigorously for five days, filtered and washed with methanol before placing the solid in a vacuum oven at 150°C to dry for 24 hours. Samples of Id Co(CN)$_x$-NaY were dried under high vacuum (10^{-4} torr) at 250, 270 and 322°C for 24 hours before being used as catalysts. The epr of the Id-270 and Id-250 zeolites had large and broad epr signals.

Ie and If   Co(CN)$_x$-NaY

Ie was made in the same way as the Id Co(CN)$_x$-NaY except that the final drying was at 95°C rather than 150°C. The epr of this species gave a strong signal indicating the presence of the cyano cobalt(III) dioxygen adduct.

If was made in the same way as Ie, except that the Co-Y was filtered, but not dried, before the addition of NaCN in methanol. The epr of If did not contain a strong epr signal of any type.

IIa and IIb   Co-Y

0.376g of CoCl$_2$·H$_2$O and 5.00g of NaY were mixed in 150ml of water overnight with vigorous stirring. The solution was filtered and dried at 150°C in

vacuo overnight. IIb Co-Y was prepared in the same way as the IIa Co-Y, but was dried at room temperature in vacuo rather than at 150°C. The dried Co-Y is very sensitive to water and will turn from blue to violet after 10 minutes exposure to air. The violet Co-Y turns to a tan after several hours exposure to air. The $Co(CN)_x$-NaY were also sensitive to water, but did not change colors as rapidly as the Co-Y.

Table 3-1
$Co(CN)_x$-NaY Cobalt and CHN analysis

Sample	%C	%H	%N	%Co
Ia	4.02	0.97	4.21	4.92
Ib	1.63	2.26	1.28	1.25
Ic	3.64	1.51	3.85	4.48
Id-250	1.05	2.34	0.45	1.20
Id-270	1.02	2.29	0.33	1.20
Id-322	0.81	2.30	0.24	1.20
Ie	1.17	1.97	1.14	1.34
If	1.02	2.30	0.85	0.77
IIa			1.71	
IIb			1.98	

Table 3-2
Formula weight and formula (wet) for the $Co(CN)_x$-NaY catalysts

Sample (fw)[a]	Formula (wet)
Ia $(16900)Na_{27.8}Co_{14.1}(NaCN)_{50.8}$	$[(AlO_2)_{56}(SiO_2)_{136}] \cdot 82H_2O$

Table 3-2--continued

Ib	$(17024)Na_{48.8}Co_{3.61}(NaCN)_{15.6}$	$[(AlO_2)_{56}(SiO_2)_{136}]\cdot192H_2O$
Ic	$(17724)Na_{29.1}Co_{13.46}(NaCN)_{48.7}$	$[(AlO_2)_{56}(SiO_2)_{136}]\cdot134H_2O$
Id-250	$(16154)Na_{49.4}Co_{3.29}(NaCN)_{5.19}$	$[(AlO_2)_{56}(SiO_2)_{136}]\cdot189H_2O$
Id-270	$(16355)Na_{49.3}Co_{3.33}(NaCN)_{3.86}$	$[(AlO_2)_{56}(SiO_2)_{136}]\cdot187H_2O$
Id-322	$(16308)Na_{49.4}Co_{3.31}(NaCN)_{2.80}$	$[(AlO_2)_{56}(SiO_2)_{136}]\cdot188H_2O$
Ie	$(16336)Na_{49.4}Co_{3.32}(NaCN)_{13.65}$	$[(AlO_2)_{56}(SiO_2)_{136}]\cdot159H_2O$ If
	$(16745)Na_{51.6}Co_{2.19}(NaCN)_{10.17}$	$[(AlO_2)_{56}(SiO_2)_{136}]\cdot193H_2O$

a. molecular weight calculated from $Na_{56-2x}Co_x(NaCN)_y\cdot Y\cdot zH_2O$ where:

$Y=[(AlO_2)_{56}(SiO_2)_{136}]$, $x=(\%Co)(mw)/5900$, $y=(\%N)(mw)/1400$,

$z=(\%H)(mw)/200$. $mw= 12752/1-[2.2(\%Co) + 35(\%N) + 90(\%H)](10^{-3})$

Table 3-3
ICP analysis for "free cobalt (II)"

sample	%free Co (II)[a]	% of Co (II) as free Co (II)	CN^-/Co (II)
Ia	0.658	13.4	3.60
Ib	1.25	b	4.32
Ic	1.39	31	3.62
Id-250	1.20	b	1.58
Id-270	1.20	b	1.12
Id-322	1.20	b	0.846
Ie	1.11	82.8	4.11

<u>Table 3-3--continued</u>

If	0.500	64.9	4.64
IIa	1.71	100	---
IIb	1.98	100	---

a. %total mass of the Co(CN)$_x$-NaY or Co-Y

b. Approximately 100% of the the cobalt was free cobalt(II).

<u>Results and Discussion</u>

<u>Co(CN)$_x$-NaY</u>

The NaY zeolite containing the cyano cobalt(II) anion [Co(CN)$_x$-NaY] functions as a free-radical initiator for the oxidation of cyclohexene and 1-hexene to their respective ene-ols and ene-ones in the neat substrate or in acetonitrile. This activity is enhanced by the presence of cobalt(II) without cyanide ligands in the NaY zeolite. The free cobalt(II) can catalyze the Haber Weiss decomposition of alkyl peroxides. The oxidation of cyclohexene to its ene-ol and ene-one by Ia Co(CN)$_x$-NaY in acetonitrile is shown in figure 3-5. No epoxide was produced in this reaction. The catalyst performs as a free radical oxidant for the oxidation of cyclohexene in acetonitrile. The blanks containing the substrate and IIa Co-Y catalyst will also oxidize cyclohexene to 1-cyclohexen-3-ol and 1-cyclohexen-3-one, albeit at a slower rate and with a lower total yield. The IIa Co-Y catalyst had 252 turnovers for 1-cyclohexen-3-ol and 858 turnovers for 1-cyclohexen-3-one in 18 hours. The "blank catalyst" [Ni(CN)$_x$-NaY zeolite] had 92.6 turnovers for the 1-cyclohexen-3-ol and 384 turnovers for the 1-hexen-3-one. When the catalyst was replaced by
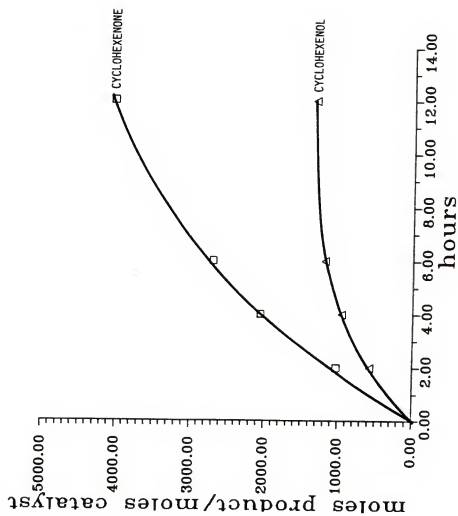
Figure 3-5   Oxidation of cyclohexene in acetonitrile by Ia Co(CN)x-NaY.

azobisisobutyronitrile (AIBN), the rate of oxidation was equivalent to that of the
la Co(CN)$_x$-NaY, suggesting that the oxidation cf cyclohexene in acetonitrile by
Co(CN)$_x$-NaY catalysts is free-radical in nature.

Oxidation reactions with norbornylene in acetonitrile also indicated that a
free-radical reaction was occurring. Norbornylene is believed to form
norbornylene oxide only in the presence of an oxygen donor and is not
normally susceptible to free-radical oxidations. After a 24 hour induction
period, we began to see a slow oxidation of norbornylene to its ketone with only
trace amounts of the epoxide.

Table 3-4
Cyclohexene oxidation turnovers in acetonitrile after 18 hours.

catalyst	1-cyclohexen-3-ol	1-cyclohexexen-3-one
la Co(CN)$_x$-NaY and AIBN	1200[a]	4000[a]
lla Co-Y	252	858
Ni(CN)$_x$-NaY	92.6	384

a. after 12 hours of reaction.

The Co-Y zeolites did not oxidize 1-hexene in the neat substrate, whereas
the Co(CN)$_x$-NaY catalysts did. This led us to believe that the cyano cobalt(III)
oxygen adduct observed in the epr was responsible for the initiation of the free-
radical oxidation of 1-hexene. The free cobalt(II) in the zeolite simply enhanced
the peroxide decomposition. This theory has some problems because the

cyano cobalt(III) oxygen adduct makes up less than 2% of the total amount of cobalt in the zeolite. The remainder of the cobalt is either free cobalt(II) or $Co(CN)_6^{3-}$ encapsulated in the supercages of the zeolite. The IR spectrum of the $Co(CN)_x$-NaY zeolite (in figure 3-6) contains a strong CN frequency at $2130cm^{-1}$. This is believed to be the CN stretching frequency for the $Co(CN)_6^{3-}$ species in the zeolite.[201,202] The $Co(CN)_x$-NaY species which were heated at elevated temperatures contain a second CN frequency at $2177cm^{-1}$ (figures 3-7 and 3-8).

At this point, we changed solvents from the neat substrate and acetonitrile to 1-methyl-2-pyrrolidinone. The oxidation of 1-hexene by $Co(CN)_x$-NaY in 1-methyl-2-pyrrolidinone gave very exciting results as seen in figure 2-2. The major product of the reaction is 1,2-epoxyhexane. The tremendous increase in selectivity for the desired product, the epoxide, indicated that a completely different type of reaction was taking place in 1-methyl-2-pyrrolidinone. In acetonitrile we had produced almost exclusively 1-hexen-3-ol and 1-hexen-3 one. The oxidation of cyclohexene by $Co(CN)_x$-NaY continued to produce the cyclohexen-3-ol and cyclohexen-3-one exclusively in 1-methyl-2-pyrrolidinone. In fact, under our conditions, we were unable to obtain the 1,2-epoxycyclohexane product from the oxidation of cyclohexene by the $Co(CN)_x$-NaY catalyst system. The autoxidation of cyclohexene by the $Co(CN)_x$-NaY is simply too rapid, under our conditions, (75°C and 50 psig oxygen) for a peroxide mechanism involving 1-methyl-5-peroxy-2-pyrrolidinone to compete.

The $Co(CN)_x$-NaY catalysts did not oxidize norbornylene in the first 48 hours of reaction in 1-methyl-2-pyrrolidinone, but four products were observed after 96
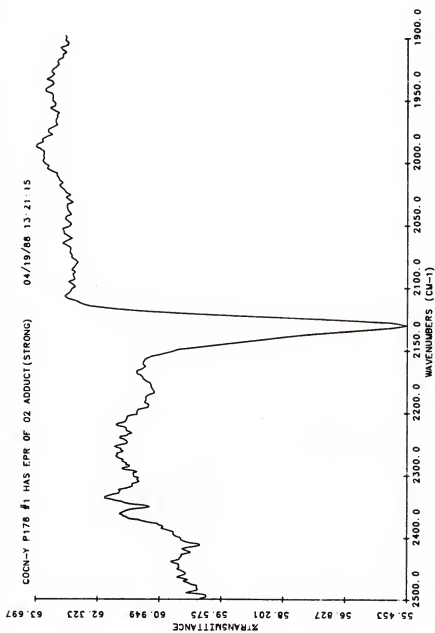
Figure 3-6   Infrared spectrum of le Co(CN)x-NaY dried at 95°C in vacuo.
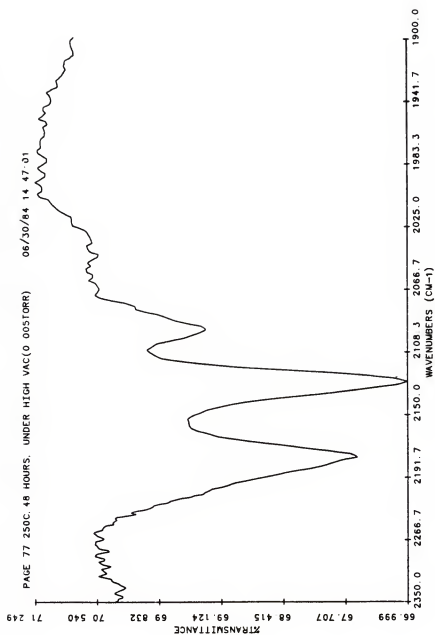
Figure 3-7   Infrared spectrum of Id-250 Co(CN)x-NaY dried at 250°C in vacuo.
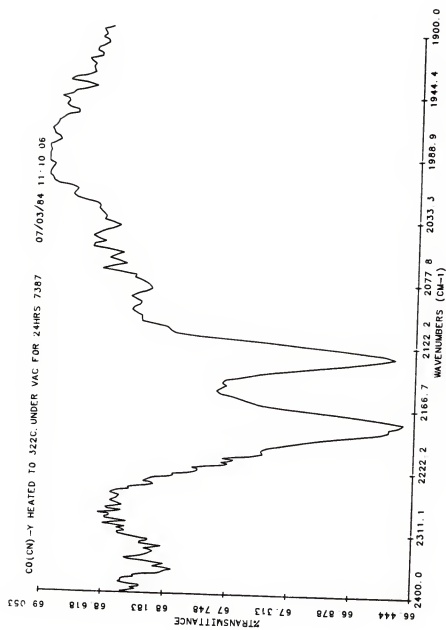
Figure 3-8 Infrared spectrum of Id-322 Co(CN)x-NaY dried at 322°C in vacuo.

hours of reaction. The endo and exo alcohols, the ketone and the epoxide were produced in a ratio of 1:1:1:18 with approximately 55 turnovers for the oxidation of norbornylene to the epoxide in 96 hours. The fact that four oxidation products were observed, and that the reaction had a 48 hour induction period, indicates that the formation of the 1-methyl-5-peroxy-2-pyrrolidinone was required, and a long induction period occurred, before the 1-methyl-5-peroxy-2-pyrrolidinone began to oxidize norbornylene.

We have explored the oxidation of alkanes and alkenes by $Co(CN)_x$-NaY and other catalysts in 1-methyl-2-pyrrolidinone and have found that most oxidations occur both to a greater extent and with more selectivity in 1-methyl-2-pyrrolidinone than in acetonitrile. The formation of the peroxide in 1-methyl-2-pyrrolidinone greatly increased the yield and the selectivity of the reactions. This may explain the activity and selectivity of reactions in 1-methyl-2-pyrrolidinone in the literature.[203]

The oxidation of cyclohexane was performed in 1-methyl-2-pyrrolidinone with the $Co(CN)_x$-NaY catalyst. This oxidation had not been successful in either acetonitrile or the neat substrate. The formation of the 1-methyl-5-peroxy-2-pyrrolidinone must, therefore, be important in the 1-methyl-2-pyrrolidinone system's ability to oxidize alkanes. In figures 3-9 and 3-10 one observes the differences in product yield beween those solutions containing the $Co(CN)_x$-NaY catalyst and the blank containing no catalyst. There were 27.5 turnovers per mole of $Co(CN)_x$-NaY catalyst, 18.8 for the conversion to the alcohol and 8.7 turnovers for the conversion to the ketone. This yielded a ratio of 2.2:1 for alcohol to ketone.
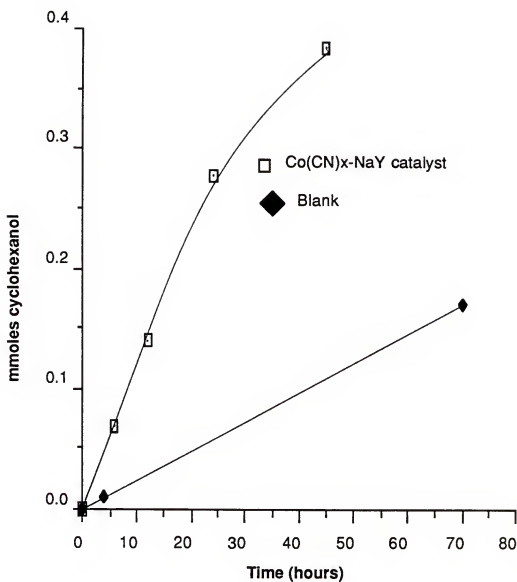
Figure 3-9 Oxidation of cyclohexane to cyclohexanol in
1-methyl-2-pyrrolidinone by Co(CN)x-NaY catalyst.
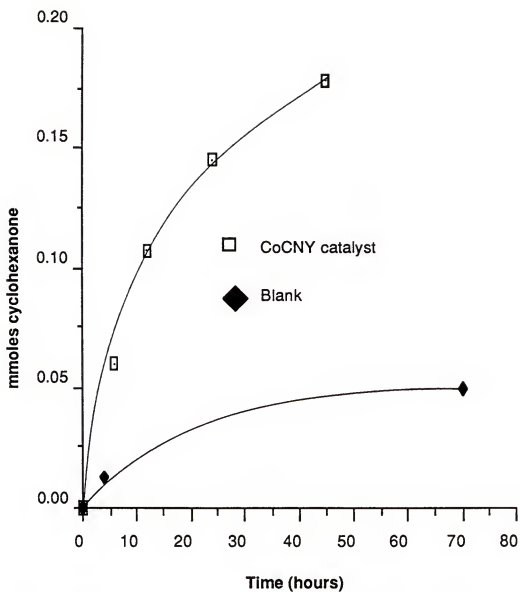
Figure 3-10 Oxidation of cyclohexane to cyclohexanone in
1-methyl-2-pyrrolidinone by Co(CN)x-NaY catalyst.

TPPMnCl Oxidations

The oxidation of cyclohexane by the porphyrin catalysts in 1-methyl-2 pyrrolidinone was not as successful because the porphyrins decomposed during the reaction. In table 3-1, it is obvious that the F_{20}TPPFeCl had the highest rate for the oxidation of cyclohexane, but figures 3-11 through 3-14 show that the TPPMnCl decomposes completely within 24 hours of the start of the reaction. The change in the visible spectrum, from figure 3-11 at time zero to that of figure 3-12 after six hours,demonstrated that the decomposition of the porphyrin begins immediately. The perfluorinated benzene rings of the F_{20}TPPFeCl protect the unsaturated portions of the porphyrin ring better than the phenyl rings of the TPPMnCl. It is, therefore, more stable to oxidation than the TPPMnCl and better able to oxidize cyclohexane. The bulk of the perfluorinated rings also helps to prevent the dimerization of the iron porphyrins discussed earlier.

Table 3-5
Cyclohexane oxidations in 1-methyl-2-pyrrolidinone[a]

Catalyst	Time (hours)	Alcohol[a]	Ketone[a]
Id-250 Co(CN)$_x$-NaY	45	19	9
F_{20}TPPFeCl[b]	7.5	26	11
TPPMnCl[b]	24	0	0

a. Turnovers in moles product per mole of catalyst.

b. Catalyst decomposed during the reaction.
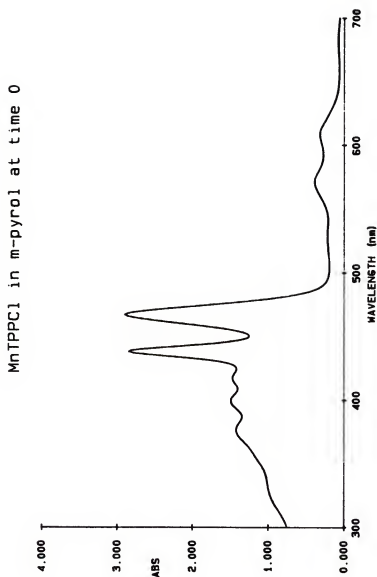
figure 3-11   Visible spectrum of TPPMnCl in 1-methyl-2
pyrrolidinone at time zero.
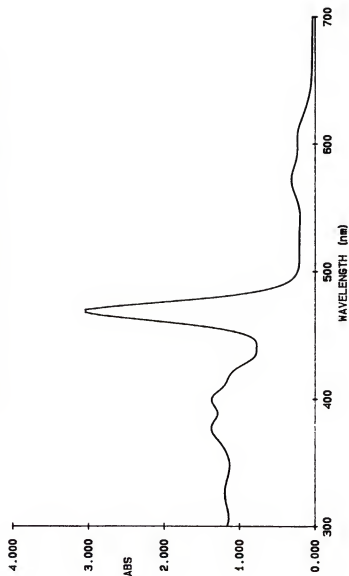
Figure 3-12   Visible spectrum of TPPMnCl in 1-methyl-2
pyrrolidinone after 6 hours at 75°C under
50 psig oxygen.
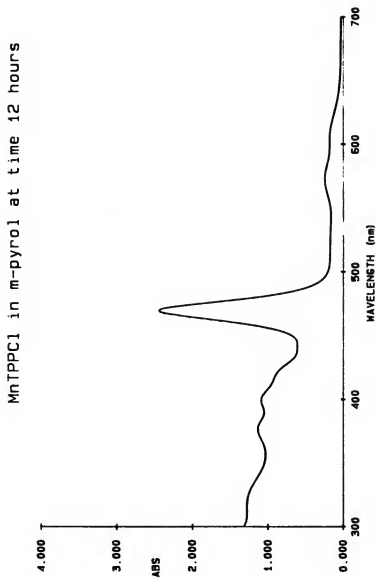
Figure 3-13   Visible spectrum of TPPMnCl in 1-methyl-2
pyrrolidinone after12 hours at 75oC under
50 psig oxygen.
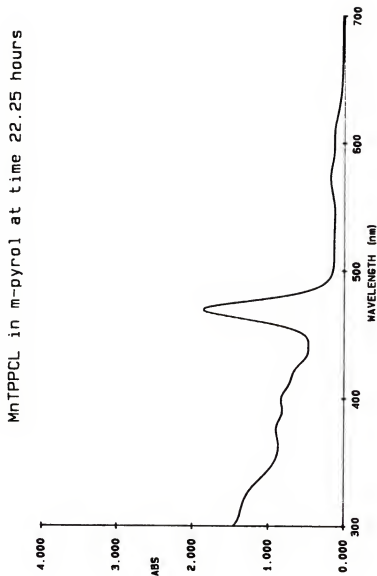
Figure 3-14   Visible spectrum of TPPMnCl in 1-methyl-2
pyrrolidinone after 22.25 hours at 75°C under 50
psig oxygen.

Experiments in which trans-beta-methylstyrene was used as the oxidative substrate were performed to pursue the oxidation of alkenes to their respective epoxides. Blanks containing the trans-beta-methylstyrene in acetonitrile and 1-methyl-2-pyrrolidinone have demonstrated that the 1-methyl-5-peroxy-2 pyrrolidinone is an effective oxygen transfer agent in the oxidation of trans-beta-methylstyrene. In acetonitrile, trace quantities of the epoxide and larger quantities of benzaldehyde (the free-radical product) were observed in the reaction mixture after 45 hours. The ratio of epoxides to benzaldehyde was 1:3 in acetonitrile. After 60 hours in 1-methyl-2-pyrrolidinone, nearly all of the trans-beta-methylstyrene has been oxidized and the ratio of epoxide to the free-radical product, benzaldehyde, was also 1:3. The styrene oxidation went to completion in 1-methyl-2-pyrrolidinone and did not in acetonitrile. The selectivity was, unfortunately, the same.

Catalysts were added to the system in order to enhance the rate and selectivity of the oxidation of trans-beta-methylstyrene in 1-methyl-2 pyrrolidinone. The first catalyst system employed was a two catalyst system consisting of TPPMnCl and $Co(CN)_x$-NaY (shown in figure 3-15). This system catalyzed the oxidation and produced the same amount of product in six hours as the blank had produced in sixty hours.

The ratio of epoxide to benzaldehyde was 3.81:1 for the two-catalyst system. The results of the trans-beta-methylstyrene oxidations are summarized in table 3-6.

Figure 3-15 trans-B-methylstyrene oxidation in 1-methyl-2-pyrrolidinone with and without Co(CN)x-NaY/TPPMnCl catalyst.

Table 3-6
Trans-beta-methylstyrene Oxidations in 1-methyl-2-pyrrolidinone

Catalyst (mg)	Time(hours)[a]	Ratio Epoxide/ Benzaldehyde	mmoles consumed/hour
none	70	0.33	0.11
TPPMnCl (21.4)	12	1.24	0.64
Co(CN)$_x$-NaY	25	1.30	0.31
[Co(CN)$_x$-NaY (100) + TPPPMnCl(20.2)]	6	3.81	1.3
AIBN(71.8)	25	3.3	0.31
MoO$_2$(acac)$_2$(230)	10	0.25	b
Mo(CO)$_6$(318)	12	0.17	b
Co(octoate)$_2$(508)	22	13.79	0.36

Oxidation of trans-beta-methylstyrene in 4:1 ethanol/1-methyl-2-pyrrolidinone

MoO$_2$(acac)$_2$(234)	24.5	0.08	b

Oxidation of trans-beta-methylstyrene in acetonitrile

none	45	0.36	b

a. All of the substrate was consumed in this time period.

b. Only a small percentage of the substrate was consumed during the reaction time period (less than 10%).

We ran oxidations containing the zeolite catalyst and the TPPMnCl by themselves with the trans-beta-methylstyrene in 1-methyl-2-pyrrolidinone to obtain mechanistic information about the TPPMnCl/Co(CN)$_x$-NaY catalyst system. The Co(CN)$_x$-NaY oxidized the trans-beta-methylstyrene rather rapidly, but the ratio of epoxide to benzaldehyde was only 1:3 (figure 3-16). An even lower yield of products was observed when the TPPMnCl was used as the catalyst, and in approximately the same ratio of epoxide to benzaldehyde as the Co(CN)$_x$-NaY (figure 3-17). These results were expected, based on the rapid increase in the formation of the 1-methyl-5-peroxy-2-pyrrolidinone when a Co(CN)$_x$-NaY catalyst is present and the rapid decomposition of TPPMnCl under these conditions in 1-methyl-2-pyrrolidinone. The increased availability of 1-methyl-5-peroxy-2-pyrrolidinone early in the reaction, due to the presence of the Co(CN)$_x$-NaY catalyst, allows the TPPMnCl catalyst to rapidly oxidize the substrate to the epoxide before it decomposes. Without the Co(CN)$_x$-NaY present, the TPPMnCl decomposes before an appreciable amount of 1-methyl 5-peroxy-2-pyrrolidinone is available for use in the epoxidation of trans-beta-methylstyrene.

The Co(octoate)$_2$ results for the oxidation of trans-beta-methylstyrene displayed in figure 3-18 show a far greater selectivity for the epoxidation of substrate than the other catalysts. This seemed to be an anomaly, until we noticed that the catalyst changed colors during the reaction. The color changed from dark blue to blue in the first four hours of reaction. The catalyst was gray after six hours, and finally turned green after 10 hours. The color change
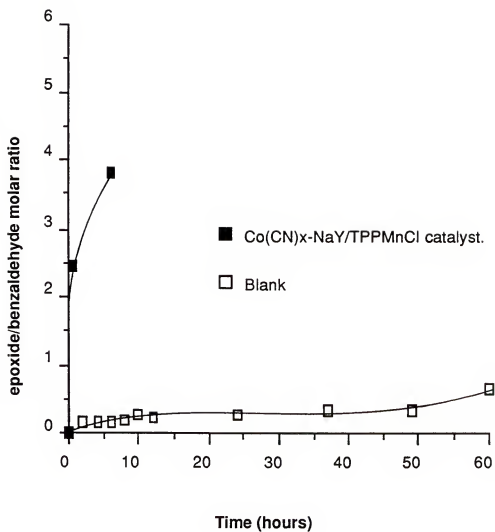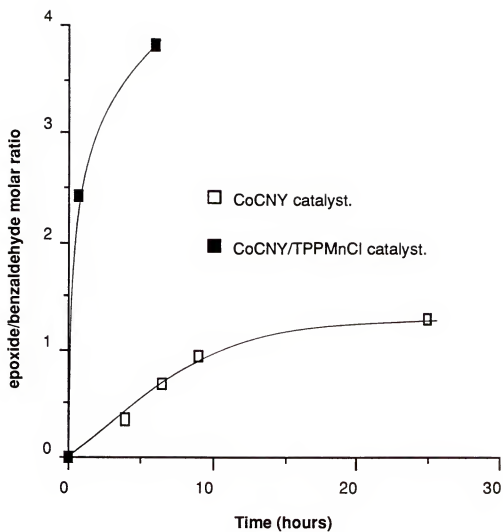
Figure 3-16 trans-B-methylstyrene oxidation in 1-methyl-2-pyrrolidinone
with Co(CN)x-NaY and Co(CN)x-NaY/TPPMnCl catalysts.
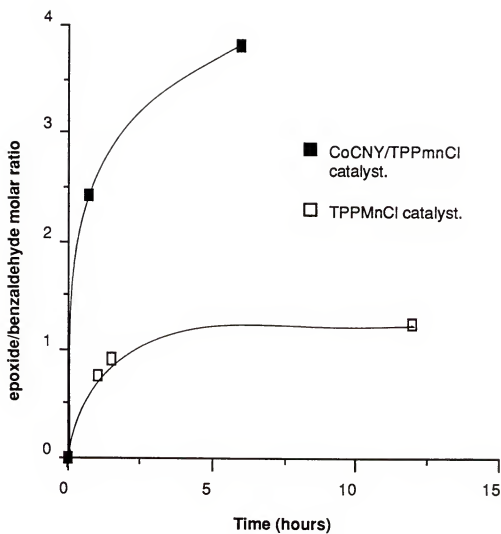
Figure 3-17 trans-B-methylstyrene oxidation in 1-methyl-2-pyrrolidinone by TPPMnCl and Co(CN)x-NaY/TPPMnCl catalyst systems.
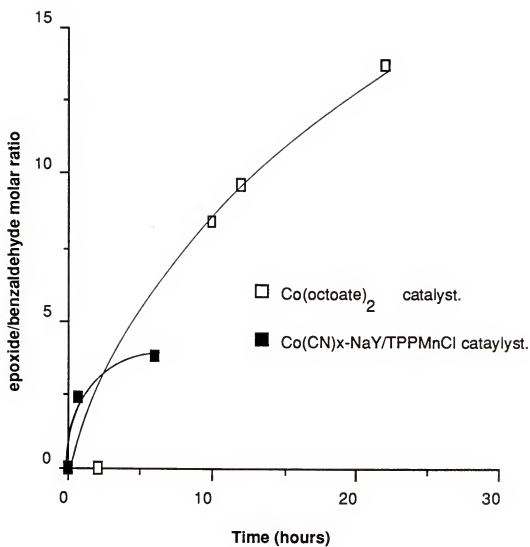
Figure 3-18 trans-B-methylstyrene oxidation in 1-methyl-2-pyrrolidinone
with Co(CN)x-NaY/TPPMnCl and Co(octoate)$_2$ catalysts.

indicated that the 1-methyl-2-pyrrolidinone had probably replaced the octoate ligands on the cobalt. The change of ligands radically increased the selectivity of the reaction since Co(octoate)$_2$ is an industrial free-radical catalyst for the non-selective oxidation of alkanes. When the Co(octoate)$_2$ was dissolved in 1-methyl-2-pyrrolidinone and left to sit on the bench exposed to air, the solution changed color from dark blue to light blue within thirty minutes. Co(1-methyl-2 pyrrolidinone)$_x$ is the most likely candidate for the resultant highly selective catalyst.

The successful oxidation of the trans-beta-methylstyrene in 1-methyl-2 pyrrolidinone by the two catalyst system encouraged us to try the same system with an alkene that is more difficult to epoxidize: 1-hexene. The solution decolorized over time and very few oxidation products of the 1-hexene substrate were found when this experiment was performed. We observed more of the oxidation products of 1-hexene after the solution had significantly decolorized. The products were a mixture of hexanols, hexanones and the epoxide. The decolorization of the solution strongly indicates that the system oxidized the TPPMnCl and inactivated it so that it could not perform as an oxygen transfer agent to the 1-hexene for the formation of the epoxide.

When used in the presence of imidazole for the oxidation of 1-hexene in 1-methyl-2-pyrrolidinone, the F$_{20}$TPPFeCl catalyst also rapidly decomposed during the reaction. The catalyst solution changed color, indicating that, after five hours of reaction and only 9.7 turnovers (turnovers = moles product/mole F$_{20}$TPPFeCl), the porphyrin ring had been oxidized by the 1-methyl-5-peroxy 2-pyrrolidinone. No reaction products were observed after this occurred.

The ratio of epoxide: 1-hexen-3-one: 1-hexen-3-ol: 2-hexanol was 6.6:1.2: 0.6: 1.3 after five hours. The results of this oxidation after 4.5 hours show a high selectivity for the epoxide (68% of the product).

The Co(CN)$_x$-NaY catayst was by itself capable of selectively oxidizing 1-hexene to the epoxide in 1-methyl-2-pyrrolidinone (figure 2-2), but died after 24 hours of reaction. This reaction was repeated in 1,5-dimethyl-2 pyrrolidinone with similar results. The graph in figure 3-19 for the oxidation of 1-hexene in 1,5-dimethyl-2-pyrrolidinone by a Co(CN)$_x$-NaY catalyst shows that the reaction was less selective in 1,5-dimethyl-2-pyrrolidinone. The efficiency of the reaction was determined by comparing it to the blank in figure 3-20. The reaction is not as selective as the previous experiments in 1-methyl-2 pyrrolidinone (figure 2-2), but one can clearly observe that the oxidation of 1-hexene occurs in 1,5-dimethyl-2-pyrrolidinone.

Heteropolyanion oxidations

In an effort to find other catalysts with higher yields and better selectivity, we tried several heteropolyanions and high-valent molybdenum and vanadium compounds. The heteropolyanions that were used had been used successfully for the oxidation of toluene with t-butyl hydroperoxide in earlier experiments.

Toluene was chosen as the oxidative substrate for the heteropolyanion reactions because it was a suitable model for the oxidation of p-xylene to terepthalic acid, which is used commercially in the synthesis of polyester resin.[204,205] The homogeneous oxidations were carried out using the substrate as the solvent with the heteropolyanion phase-transferred into toluene by tetraalkylammonium bromide salts. The two most effective phase-transfer
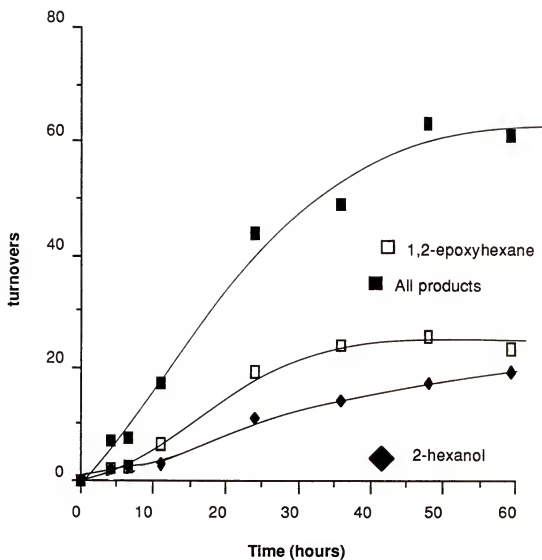
Figure 3-19 Catalytic oxidation of 1- hexene in
1,5-dimethyl-2-pyrrolidinone by p178 #1 Co(CN)x -NaY
catalyst.
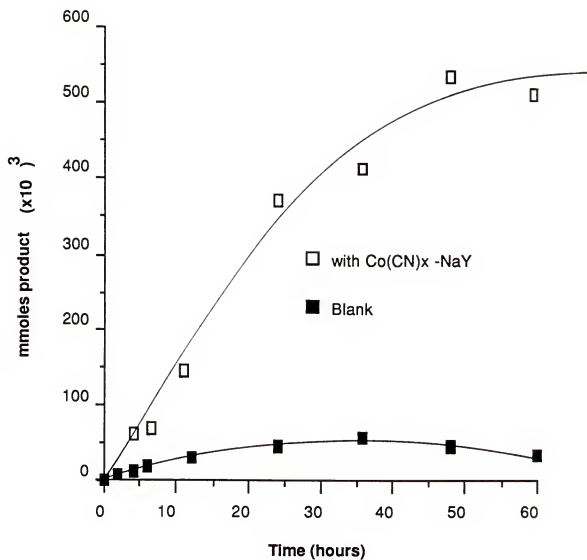
Figure 3-20   Oxidation of 1-hexene in 1,5-dimethyl-2
pyrrolidinone with and without Co(CN)x -NaY.

agents for the heteropolyanions were tetraheptylammonium bromide and methyl trioctylammonium bromide. The methyl trioctylammonium salts were slightly more effective due to their greater solubility in toluene.

In an attempt to perform more selective oxidations of the alkenes, sodium hypochlorite, an oxygen transfer agent, was used as an oxygen source. Unfortunately, the hypochlorite violently decomposed the heteropolyanions and no oxidation products were observed. Attempts to oxidize toluene to benzaldehyde with molecular oxygen also failed, as did attempts to use hydrogen peroxide as the oxidant. The heteropolymolybdates rapidly decomposed in the presence of hydrogen peroxide and the heteropolytungstates were not reactive in the presence of hydrogen peroxide.

The decomposition of the heteropolymolybdates leads one to believe that the oxidation of organic substrates by the combination of a molybdate and hydrogen peroxide can best be performed by the method of Trost,[99] which uses polymeric molybdates without the heteropolyanion type structure or organization. Others in the literature have also pointed out the decomposition of the heteropolyanions during the catalytic oxidation of substrates.[56]

Our results (tables 3-7, 3-8 and 3-9), however, compare favorably with those of Matveev[206,207] Eberson[53-55], and Jonson[56] for the oxidation of toluene. The oxidation of toluene to benzaldehyde without the concommitant formation of phenyl-p-tolylmethane is an improvement in selectivity over the processes involving the air oxidation of toluene by heteropolyanions in which as much as 77% of the product is the phenyl-p-tolylmethane.[208] The $Mn^{IV}Mo_9O_{32}^{6-}$ was an effective catalyst for the oxidation of organic substrates, but decomposed

Table 3-7

Oxidation of toluene by $[CrMo_6O_{24}H_6]^{3-}$ with t-BuOOH

Heteropolyanion (mmoles)	t-BuOOH (mmoles)	Time (hours)	Temperature (°C)	Benzaldehyde (mmoles)	Mole % (relative to hpa)
0.3765	0.60	24	22	0.46	122
0.407	0.60	24	115	0.50	123
0.408	0.30	24	35	0.555	136
"	"	48	"	0.63	154
"	"	72	"	0.63	154
0.411	0.30	24	62	0.39	95
"	"	48	"	0.39	95
"	"	72	"	0.52	127

during the reaction to Mn(II) and molybdates.[56] All attempts to selectively epoxidize alkenes with the heteropolyanions in acetonitrile or the neat substrate with t-butyl hydroperoxide were unsuccessful. The oxidation of alkenes by the heteropolyanions produced a myriad of free-radical oxidation products.

Although the oxidation of toluene by alkyl hydroperoxides with heteropolyanions was a more selective reaction than those heteropolyanion processes which used air as an oxidant, we were unable to obtain the large catalytic yields which were expected from the heteropolyanion oxidations. All attempts to further enhance the activity of the heteropolyanion catalysts either destroyed the heteropolyanion structure or failed to increase the product yield and enhance the rate of reaction.

Table 3-8
Oxidation of toluene by heteropolyanions with alkyl hydroperoxides[a]

Heteropolyanion (mmoles)	Temperature (^{o}C)	Benzaldehyde (mmoles)	Mole% (relative to hpa)
MoO_4^{2-}(1.38)	23	0	0
$MnMo_9O_{32}^{6-}$(0.354)	56	0.684	193
$Co_2W_{12}O_{42}^{8-}$(0.154)	23	0.226	147

(a) All of the catalysts were reacted with 1.50mmoles of t-BuOOH for 24 hours.

Table 3-9

Oxidation of toluene by $[CrMo_6O_{24}H_6]^{3-}$ and t-BuOOH
in the presence of methanol

Time	Temperature	Benzaldehyde	Mole%
(hours)	(^{o}C)	(mmoles)	(relative to hpa)
24	59	0.27	66
48	59	0.25	61
72	81[b]	0.38	93
96	81	0.41	100

(a) 0.411mmoles of hpa catalyst, 0.30mmoles t-BuOOH, and 9.9mmoles of methanol were used in this reaction. (b) Temperature was raised from 59°C to 81°C after 48 hours.

The oxidation of alkenes by the heteropolyanions in 1-methyl-2 pyrrolidinone was surprisingly unsuccessful. The work by Hill[98] with heteropolyanions and iodosylbenzene indicated that these species were good oxidation catalysts. The fact that the heteropolyanions with t-butyl hydroperoxide were capable of oxidizing toluene to benzaldehyde led us to believe that they would be excellent catalysts for the oxidation of alkenes with 1-methyl-5 peroxy-2-pyrrolidinone. This was not true. In a 48 hour time period, $(NH_4)_6MnMo_9O_{32}$ did not oxidize 1-hexene at all. The $H_3PMo_{12}O_{40}H_2 \cdot 14H_2O$ and $(NH_4)_3CrMo_6O_{24}H_6 \cdot 8H_2O$ did not produce product in high yields (figures 3-21 and 3-22) as expected. The $H_3PMo_{12}O_{40}H_2 \cdot 14H_2O$ produced only 1-hexen-3-one and 1-hexen-3-ol.
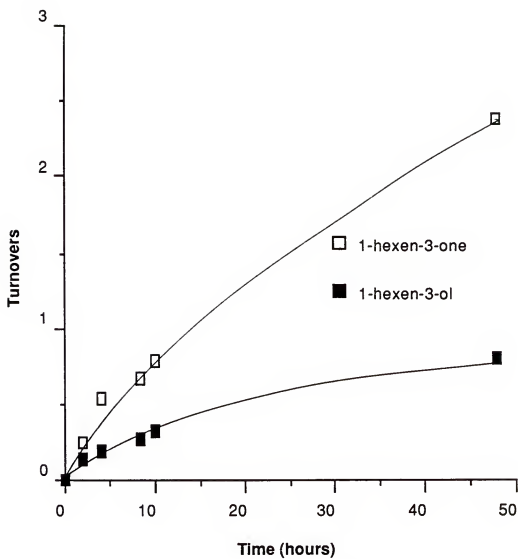
Figure 3-21 Oxidation of 1-hexene in 1-methyl-2-pyrrolidinone by 12-molybdophosphoric acid (172mg)
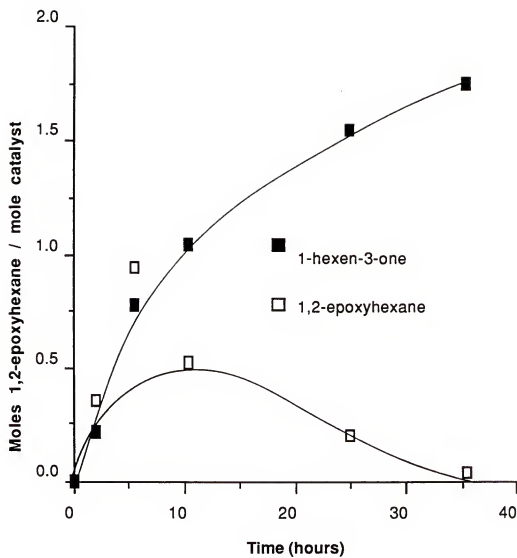
Figure 3-22 Oxidation of 1-hexene in 1-methyl-2-pyrrolidinone by
ammonium 6-molybdochromium (III) (326mg).

The epoxide was not an observed product. The $(NH_4)_3CrMo_6O_{24}H_6 \cdot 8H_2O$ did produce the epoxide. After six hours,however, the catalyst decomposed and stopped producing the epoxide and began to decompose the epoxide that had been produced earlier in the reaction.

The heteropolyanions used in the toluene oxidation experiments did not have peaks in their respective voltammograms. These heteropolyanions included: $Co_2W_{11}O_{39}^{8-}$, $MnMo_9O_{32}^{6-}$, $MnPW_{11}O_{39}^{4-}$, and the $Fe(OH_2)SiW_{11}O_{39}^{5-}$. This group also surprisingly, included the $CrMo_6O_{24}H_6^{3-}$ heteropolyanion in both the fresh pink alkylammonium salt and the reduced brown salt. This is strong evidence that the reduction of the pink 6-molybdochromium(III) is irreversible and explains why there were so few turnovers in this reaction.

The method of phase-transferring the heteropolyanions with an excess of methyltrioctylammonium bromide made the measurement of oxidation potentials more difficult. Potentials greater than +0.60V could not be measured because of the large oxidation potentials at 0.779V and 1.12V and the reduction potential at +0.963V for the alkylammonium salt. The potential region between 0.60V and -1.60V did not contain peaks due to the alkylammonium salt. Discussion of the oxidation and reduction potentials of the heteropolyanions is, therefore, limited to the peaks falling within this region. The voltammogram for methyltrioctylammonium bromide is shown in figure 3-23.

The heteropolyanions which had quasi-reversible waves were $H_3PW_{11}O_{39}$ (figure 3-24), $Rh_2GeW_{11}O_{39}^{4-}$ (figure 3-25), and $RuGeW_{11}O_{39}^{6-}$ (figures 3-26 and 3-27). Our group has successfully used the rhodium and ruthenium
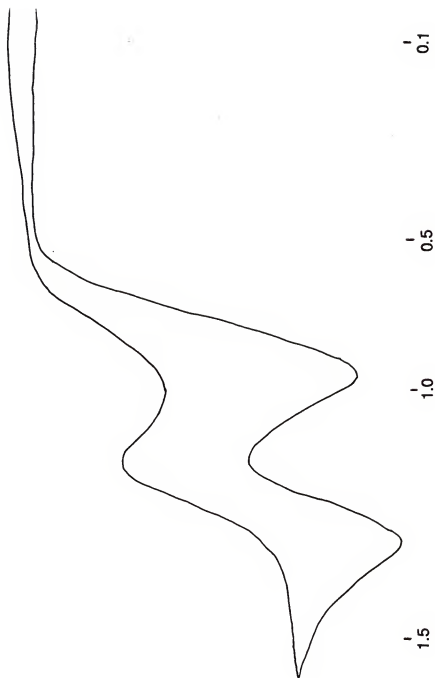
Figure 3-23   Cyclic voltammogram of
methyltrioctylammonium bromide from +1.5V
to +0.1V.
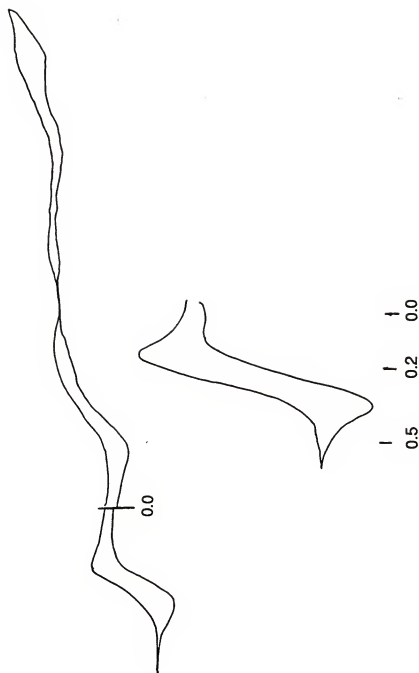
Figure 3-24   Cyclic voltammogram of 11-phosphotungstic acid from +0.5V to 0.0V and from +0.5V to -1.6V.

0.0   -0.5   -1.0   -1.5
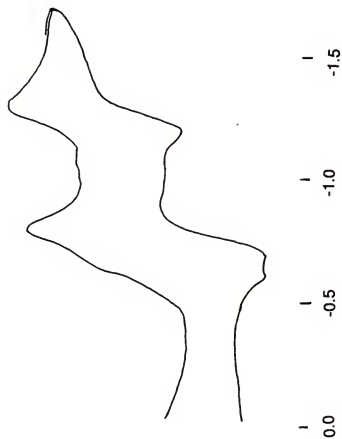
Figure 3-25   Cyclic voltammogram of 11-tungstogermanate
bis rhodium (III) from 0.0V to -1.5V.
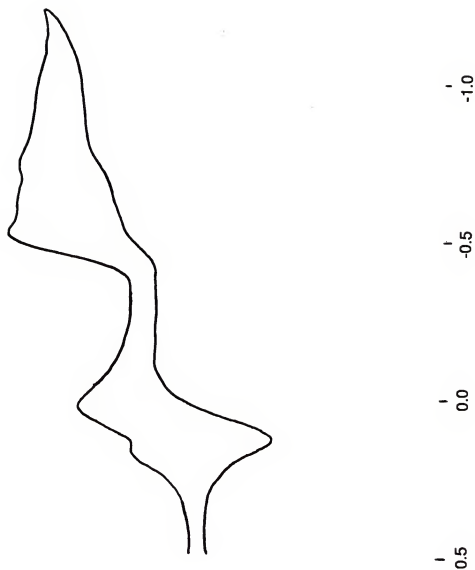
Figure 3-26   Cyclic voltammogram of purple
11-tungstogermanate ruthenium (III) from
+0.5V to -1.0V.
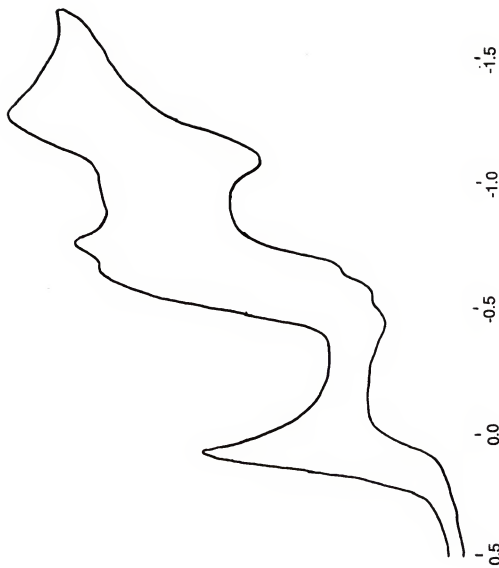
Figure 3-27   Cyclic voltammogram of black-green
11-tungstogermanate ruthenium (III)
from +0.5V to -1.0V.

11-tungstogermanates with molecular oxygen for the oxidation of alkenes. The
11-tungstophosphate has been used by Hill for the catalytic photochemical
dehydrogenation of alkanes.[97,108] These three heteropolyanions had
voltammograms containing quasi-reversible reduction potentials between
+0.60V and -1.60V.

$MoO_2(acac)_2$ (where acac = acetylacetonate) (figure 3-28) and $Mo(CO)_6$
(figure 3-29) showed greater activity in the oxidation of 1-hexene than did the
heteropolyanions, producing a ratio of approximately 2:1 of 1,2-epoxyhexane to
other products after 8 hours. $VO(acac)_2$ showed no activity for the oxidation of
1-hexene after 20 hours at 75°C under 50 psig oxygen. These results were
expected, since the literature reports that vanadium catalysts are approximately
100 times less active than the molybdenum catalysts for the epoxidation of
olefins by alkyl hydroperoxides.[54] The oxidation of 1-hexene in 1-methyl-2
pyrrolidinone was also performed using $MoO_2(acac)_2$ with BaO present (figure
3-30). The BaO stabilized the 1-methyl-5-peroxy-2-pyrrolidinone so that the
catalyst did not decompose the peroxide to the succinimide. This allows the
molybdenum peroxide complex to form and become the oxidizing species. The
product yield of 1,2-epoxyhexane from this reaction was only slightly more than
stoichiometric, but the selectivity was 100%. This result matches a previous
literature report[67] in which cumene hydroperoxide was added to the substrate
and catalyst at 120°C. Our oxidation was performed at 75°C with the peroxide
produced in situ during the reaction.

The $MoO_2(acac)_2$ proved to be a poor catalyst for the oxidation of butyl
sulfide (figure 3-31). It did not oxidize the butyl sulfide as rapidly as either the
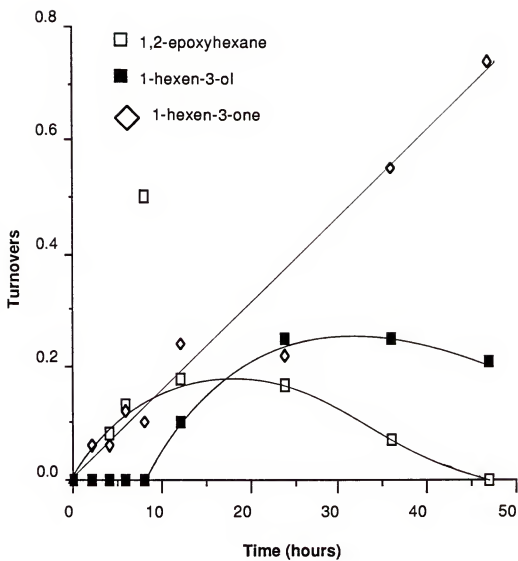
Figure 3-28   Oxidation of 1-hexene in 1-methyl-2-pyrrolidinone by molybdenyl acetylacetonate (147mg).
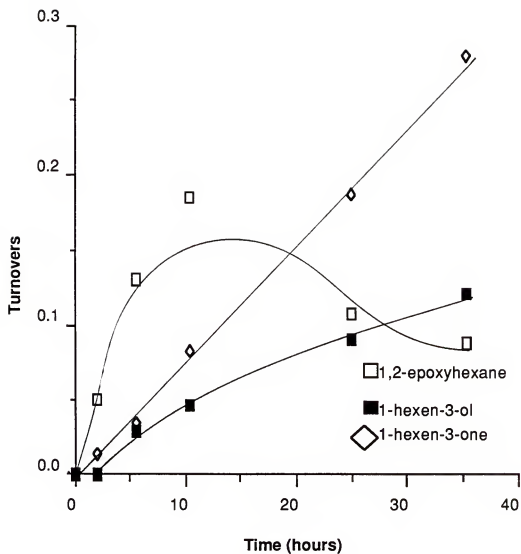
Figure 3-29 Oxidation of 1-hexene in 1-methyl-2-pyrrolidinone
by molybdenum hexacarbonyl (183mg).
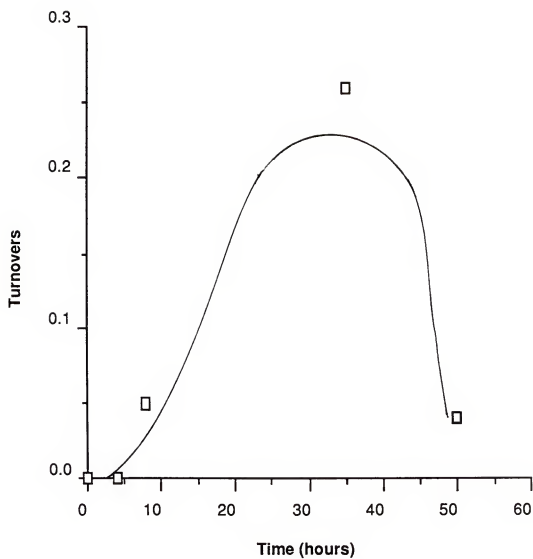
Figure 3-30   1-hexene oxidation by $MoO_2(acac)_2$ (101mg)/BaO in 1-methyl-2-pyrrolidinone.
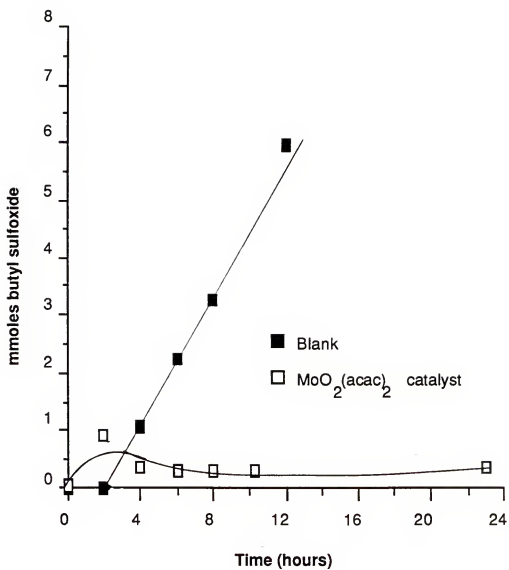
Figure 3-31 Oxidation of butyl sulfide with molybdenyl acetylacetonate
catalyst and without catalyst in 1-methyl-2-pyrrolidinone.

TPPMnCl or the $Co(CN)_x$-NaY catalysts.

The oxidation of butyl sulfide in 1-methyl-2-pyrrolidinone without catalyst proceeded rather slowly (shown in figure 3-32) when compared to the catalyzed reactions in figures 3-33 through 3-35. In the first eight hours, the reaction without catalyst present produced only the butyl sulfoxide and, after 12 hours, only small quantities of the butyl sulfone were detected.

When $Co(CN)_x$-NaY and TPPMnCl (figures 3-33 and 3-34 respectively) were added as catalysts for the reaction, the rate of reaction increased dramatically as well as the quantity of butyl sulfone produced. When the $Co(CN)_x$-NaY and TPPMnCl catalysts were used together, the rate of reaction doubled and the ratio of sulfoxide to sulfone increased. In table 3-10, it is obvious that the $Co(CN)_x$-NaY/TPPMnCl mixed catalyst system was the most effective for the oxidation of butyl sulfide to its sulfoxide.

The TPPMnCl and $Co(CN)_x$-NaY catalysts were not as individually effective or selective for the oxidation of butyl sulfide to butyl sulfoxide as they were together. The oxidation of butyl sulfide is not free-radical in nature. It is an oxygen-transfer reaction in which an activated oxygen atom is transferred from either the 1-methyl-5-peroxy-2-pyrrolidinone, slowly, or, more rapidly, from a catalyst. What probably occurred in the TPPMnCl/$Co(CN)_x$-NaY catalyst system was that the $Co(CN)_x$-NaY oxidized the 1-methyl-2-pyrrolidinone to 1-methyl-5 peroxy-2-pyrrolidinone and the peroxide then formed a metal-peroxide species with the TPPMnCl.

This species in turn oxidized butyl sulfide selectively to the sulfoxide, rather than the sulfone. This contradicts what was proposed by Mansuy,[172] but
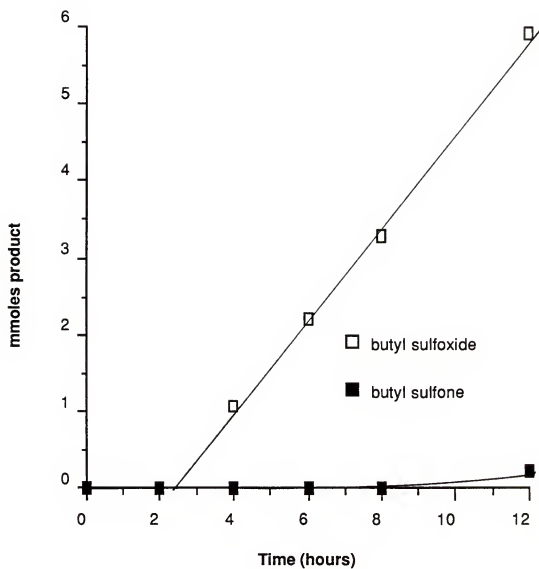
Figure 3-32 Oxidation of butyl sulfide in 1-methyl-2-pyrrolidinone without catalyst.
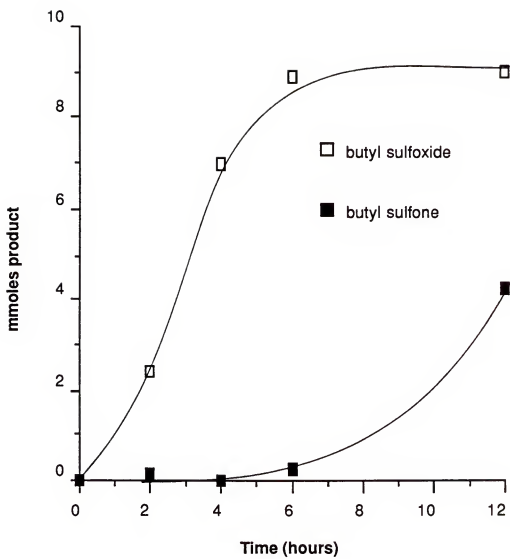
Figure 3-33 Oxidation of butyl sulfide in 1-methyl-2
pyrrolidinone by Co(CN) x-NaY catalyst.
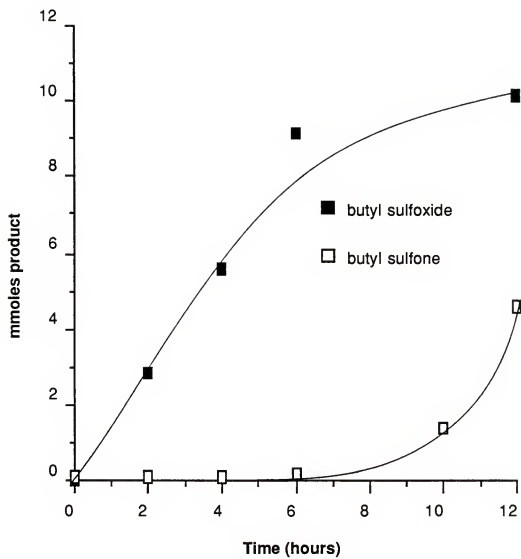
Figure 3-34 Oxidation of butyl sulfide in 1-methyl-2-pyrrolidinone by TPPMnCl.
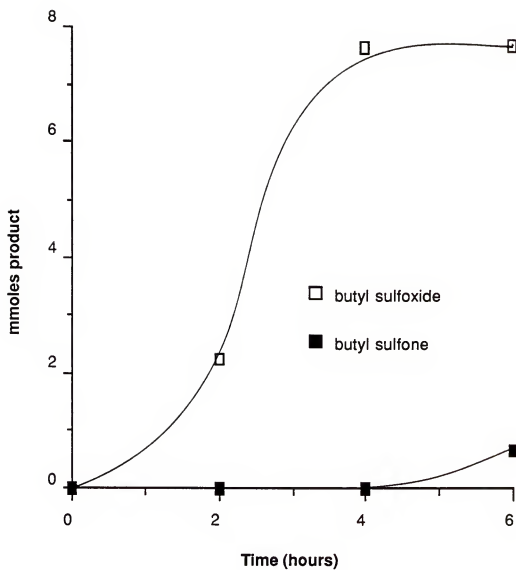
Figure 3-35 Oxidation of butyl sulfide in 1-methyl-2-pyrrolidinone by
a Co(CN)x-NaY/ TPPMnCl catalyst.

seems to fit the butyl sulfide and trans-beta-methylstyrene data better than the
free-radical mechanism proposed by Mansuy.

Table 3-10

Butyl Sulfide Oxidations in 1-methyl-2-pyrrolidinone

Catalyst (mmoles)	Sulfoxide/sulfone at reaction completion	mmoles Bu$_2$S consumed per hour[a]
MoO$_2$(acac)$_2$ (0.54)	b	c
TPPMnCl (0.033)	2.2	1.4
Co(CN)$_x$-NaY[d] (0.025)	2.1	1.4
TPPMnCl/Co(CN)$_x$-NaY[d] (0.028)/(0.023)	11.8	2.8
none	25.8	0.70

(a) Measured from: 3ml Bu$_2$S (16.7mmoles)/time in which all Bu$_2$S was
consumed. (b) No sulfone produced within 24 hour time period. (c) Was not
measurable because the sulfoxide was oxidized to products other than butyl
sulfone. (d) Id-270 Co(CN)$_x$-NaY

Conclusion

The Co(CN)$_x$-NaY catalysts which were active for the oxidation of alkenes were the same Co(CN)$_x$-NaY catalysts which increased the oxidation of mp in chapter 1: Ia, Id-250, Id-270 and Ie. The Co(CN)$_x$-NaY catalysts with little or no epr signal were not good catalysts for the oxidation of alkenes: Ic and If. The Co-Y catalysts were not capable of forming the cyano cobalt(III) dioxygen adduct, and did not exhibit the same oxidation activity as the Co(CN)$_x$-NaY catalysts (which had epr signals) for the oxidation of 1-hexene.

The cyanide/cobalt ratio did not seem to be an important factor in the activity of the Co(CN)$_x$-NaY catalysts. The active catalysts had cyanide to cobalt ratios between 1.12 and 4.11, and the inactive catalysts had cyanide to cobalt ratios between 0.846 and 4.64.

The third factor, which effected the activity of the catalysts, was the percentage of cobalt as free cobalt in the Co(CN)$_x$-NaY catalysts. All of the cobalt in the Id Co(CN)$_x$-NaY catalysts (which were dried at elevated temperatures in vacuo) was free cobalt and, excluding the catalyst which was heated to 322°C, these catalysts were the most active for the oxidation of alkenes. Ia had only 13.4% free cobalt and was not active for the oxidation of 1-hexene. Ia also had 14.1 cobalt per formula weight, however, which caused steric crowding in the supercages and possibly blocked the substrates' access to the interior of the zeolite. If this is true, the oxidation of cyclohexene may take place on the outer surface of the Y zeolite. This would explain why all of the Co(CN)$_x$-NaY and Co-Y catalysts were capable of oxidizing cyclohexene at

higher rates than the blank oxidations.

We found that the best catalyst system for the oxidation of trans-beta-methylstyrene and butyl sulfide was the $Co(CN)_x$-NaY/TPPMnCl co-catalyst system. The highest rates of reaction and the highest selectivity were found for this catalyst system. This was most likely due to the increase in the rate of formation of 1-methyl-5-peroxy-2-pyrrolidinone, caused by the $Co(CN)_x$-NaY, which allowed the TPPMnCl to react with the peroxide prior to its decomposition. The use of protected porphyrins, particularly those synthesized by Traylor,[159-62] should greatly increase the yield of oxidation products.

The $MoO_2(acac)_2$ and the $Mo(CO)_6$ catalysts were not good catalysts for these reactions. Their oxidation selectivity and yield were very low. The selectivity of the $MoO_2(acac)_2$ was greatly increased, however, when BaO was added to the reaction.

The heteropolyanions selectively oxidized toluene to benzaldehyde with alkylhydroperoxides only when the heteropolyanion contained heteroatoms with large oxidizing potentials, such as chromium(III) or manganese(IV). These powerful oxidizing heteroatoms were very difficult to reoxidize, and their reduction was often accompanied by the decomposition of the heteropolyanion structure. $MnMo_9O_{32}^{6-}$, for example, decomposed to Mn(II) and polymolybdates during the oxidation of toluene.[56] The cyclic voltammograms of these compounds indicated that the reduction of this type of heteropolyanion was irreversible on the cyclic voltammetry time scale. Voltammograms of the ruthenium and rhodium 11-tungstogermanates had quasi-reversible waves which explained why they were capable of catalyzing the oxidation of alkenes

in the presence of molecular oxygen. They were more readily reoxidized to their highest oxidation state during the course of the reaction and were, therefore, capable of more than one or two turnovers. The catalysts containing phosphorus or silicon, primary heteroatoms with iron, manganese, cobalt or chromium, secondary heteroatoms were capable of no more than one or two turnovers. The cyclic voltammetry shows that only those type III heteropolyanions[97,108] which had reversible or quasi-reversible waves were suitable catalysts for the oxidation of alkenes with molecular oxygen.

The asymmetric epoxidation of alkenes may be possible with chiral amide peroxides formed from the 5-substituted 1-methyl-2-pyrrolidinone. Both 1-methyl-2-pyrrolidinone and 1,5-dimethyl-2-pyrrolidinone were capable of generating amide peroxides at 75°C under 50 psig oxygen and these peroxides were capable of oxidizing alkenes in conjunction with oxidation catalysts.

CHAPTER 4
CONCLUSIONS

The reaction of O_2 with neat 1-methyl-2-pyrrolidinone and 1,5-dimethyl-2 pyrrolidinone at 75°C under 50 psig of molecular oxygen was shown by titration with thiosulfate to produce a large quantity of an oxidizing species which was identified through nmr, IR and GC-MS. An induction period is observed suggesting an autoxidation mechanism. By contrast, under the same conditions, 2-pyrrolidinone did not generate an oxidizing species and furthermore the catalyzed reaction of alkenes with O_2 in this solvent did not occur under these conditions. The reaction of N-methylmorpholine with O_2 under these conditions does not form an oxidizing species and we note that reaction to form the N-oxide is reported at higher temperatures and pressures.[1] At 75°C, N-methylmorpholine decomposed to a brown solid.

The next substrate was selected to model functionality resembling 1-methyl-2-pyrrolidinone in a polypeptide. The involvement of peroxides in the P-450 shunt prompted an investigation of this system. When the amino acid proline reacts to form a polypeptide or protein, the $OC-N(CH_3)R$ functionality is introduced into the polymer. This is modeled by the acetylated L-prolinamide. Tests for peroxide gave positive results for peroxide only in the oxidized solutiion of the acylated prolinamide and none for the attempted L-prolinamide reaction. This result is consistent with only the CH_2 or CH of the alkyl amide of the pyrrolidinone ring being readily oxidized by O_2 to the peroxide at low

the pyrrolidinone ring being readily oxidized by O_2 to the peroxide at low temperatures and pressures.

The possibility of P-450 catalyzed oxidation of proline type residues in proteins and polypeptides as well as catalyzed reactions of O_2 with other biological reducing substrates[209] to form hydroperoxides must be considered as candidates for involvement in the shunt mechanism of the P-450 cycle.

The catalytic oxidation of alkenes, alkanes and alkyl sulfides strongly indicated that the 1-methyl-5-peroxy-2-pyrrolidinone is a good source of hydroperoxide and in conjunction with metal catalysts it is capable of oxidizing organic substrates.

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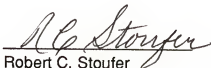209. Baumstark, A.L. *Bioorg. Chem.* **1986**, *14*, 326

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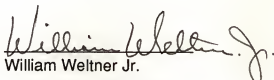
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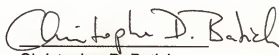
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